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Załącznik nr 3

**Autoreferat w języku angielskim
do wniosku o przeprowadzenie procedury habilitacyjnej**

Scientific Curriculum Vitae

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1. Personal data

Krzysztof Piotr Kilian

2. Qualifications

- 1998 | **M.Sc.**, Interfaculty Program in Environmental Protection, University of Warsaw.
Thesis title: „Bream (*Abramis brama L.*) as biomonitoring species in Polish Environmental Specimen Bank”, supervisor: prof. dr hab. Jerzy Golimowski.
- 2004 | **PhD**, Faculty of Chemistry, University of Warsaw.
Thesis title: „Application of porphyrin ligands for complexing and preconcentration of metal ions”, supervisor: prof. dr hab. Krystyna Pyrzyńska
- 2014 | Certificate in Radiopharmaceutical Chemistry/Radiopharmacy, ETH Zurich.

3. Information on employment in scientific institutions

2004-present University of Warsaw

including:			
from	to		
10.2004	01.2007	Faculty of Chemistry	assistant professor
02.2007	09.2017	Heavy Ion Laboratory	assistant professor
04.2010	12.2012	Center of Preclinical Studies UW	deputy director
01.2013	06.2017	Center of Preclinical Studies UW	director
07.2017	present	Biological and Chemical Research Centre UW	head of the CePT Lab
10.2017	present	Heavy Ion Laboratory	senior scientific officer

4. Achievements resulting from Art. 16 item 2 of the act of 14 March 2003 on scientific degrees and scientific title on scientific degrees and titles in the field of arts (Dz.U.nr 65, poz.595)

4.1 Habilitation-topic title

Static and flow methods of isolation and preconcentration of metal ions on solid sorbents - analytical and radiochemical applications

4.2 Publications selected for the habilitation process:

H1.Knap, M., **Kilian, K.**, Pyrzyńska, K. [✉] *On-line enrichment system for manganese determination in water samples using FAAS* (2007) *Talanta*, 71 (1), 406-410.

My contribution: design, methodology; experimental: sorbent synthesis, design and construction of the flow system, determination of sorbent characteristics, AAS analysis, interference analysis, analysis of water samples; data analysis; preparation of the manuscript.

My contribution: **70%**

IF₂₀₁₈=4,244¹⁾ IF_(as issued)=3,374²⁾ MNiSW=40³⁾ Cited: 20⁴⁾

H2.Pyrzyńska, K. [✉], **Kilian, K.** *On-line sorption-based systems for determination of cadmium with atomic spectrometry detectors* (2007) *Water Research*, 41 (13), 2839-2851.

My contribution: design the review and work structure; selecting literature in the "Flow systems" and "Column packing" sections; a critical review of literature; data analysis in the "Comparison of the flow systems" section and the preparation of the manuscript.

My contribution: **40%**

IF₂₀₁₈=7,051 IF_(as issued)=3,3427 MNiSW=45 Cited: 39

H3.**Kilian, K.** [✉], Pyrzyńska, K. *Affinity of some metal ions towards 1,8-diaminonaphthalene conductive polymer* (2008) *Reactive and Functional Polymers*, 68 (5), 974-980.

My contribution: design, methodology; experimental: sorbent synthesis, design and construction of the system, determination of sorbent characteristics, AAS determination, interference analysis; data analysis; preparation of manuscript; corresponding author.

My contribution: **80%**

IF₂₀₁₈=2,975 IF_(as issued)=2,039 MNiSW=35 Cited: 13

H4. Rutkowska, J., **Kilian, K.**, Pyrzyńska, K. [✉] *Removal and enrichment of copper ions from aqueous solution by 1,8-diaminonaphthalene polymer* (2008) *European Polymer Journal*, 44 (7), 2108-2114.

My contribution: design, methodology; experimental: sorbent synthesis, design and construction of a preconcentration system, determination of sorbent characteristics, AAS determination, interference analysis; data analysis; preparation of the manuscript.

My contribution: **70%**

IF₂₀₁₈=3,741

IF_(as issued)=2,143

MNiSW=35

Cited: 18

H5. **Kilian, K.** [✉], Pęgier, M., Pękal, A., Pyrzyńska, K. *Distribution and isolation of metallic and radionuclidic impurities in the production of 18F-fluorodeoxyglucose* (2016) *Journal of Radioanalytical and Nuclear Chemistry*, 307 (2), 1037-1043.

My contribution: design, methodology; experimental: synthesis and collection of samples for tests, calibration of germanium detector; development of measurement methodology, spectra registration, identification of impurities and calculation of activity; data analysis; preparation of the manuscript, corresponding author.

My contribution: **50%**

IF₂₀₁₈=1,181

IF_(as issued)=1,282

MNiSW=15

Cited: 1

H6. **Kilian, K.** [✉], Pyrzyńska, K., Pęgier, M. *Comparative Study of Sc(III) Sorption onto Carbon-based Materials* (2017) *Solvent Extraction and Ion Exchange*, 35 (6), 450-459.

My contribution: design, methodology; experimental: characterization of sorbents using the Boehm method, static experiments, determination of sorption parameters according to selected models; data analysis; preparation of the manuscript, corresponding author.

My contribution: **60%**

IF₂₀₁₈=2,034

IF_(as issued)=2,456

MNiSW=25

Cited: 0

H7. Pęgier, M., **Kilian, K.** [✉], Pyrzyńska, K. *Enrichment of scandium by carbon nanotubes in the presence of calcium matrix* (2018) *Microchemical Journal*, 137, 371-375.

My contribution: design, methodology; experimental: static experiments, sorption of the scandium in the column procedure, analytical parameters, Ca²⁺ distribution; data analysis; preparation of the manuscript, corresponding author.

My contribution: **60%**

IF₂₀₁₈=2,746

IF_(as issued)=2,746

MNiSW=35

Cited: 0

H8. Pyrzyńska K., **Kilian K.**[✉], Pęgier M., *Isolation and purification of scandium: From industry to medicine*, (2019) *Isolation & Purification Reviews*, 48:1, 65-77.

My contribution: design the review and work structure; selecting literature in the "Radiochemical isolation of scandium" section; a critical review of literature; preparation of the manuscript, corresponding author.

My contribution: **40%**

IF₂₀₁₈=4,212

IF_(as issued)=4,212

MNiSW=45

Cited: 1

H9. **Kilian K.**[✉], Cheda L., Sitarz M., Szkliniarz K., Choiński J., Stolarz A.; *Isolation of ⁴⁴Sc from Natural Calcium Carbonate Targets for Synthesis of ⁴⁴Sc-DOTATATE*, (2018) *Molecules*, 23, 1787;

My contribution: design, methodology; experimental: isolation of scandium from the target material, selection of sorbent and conditions, synthesis and quality control ⁴⁴Sc-DOTATATE; data analysis; preparation of the manuscript corresponding author.

My contribution: **60%**

IF₂₀₁₈=3,098

IF_(as issued)=3,098

MNiSW=30

Cited: 1

Bibliometric parameters of scientific publications selected for the habilitation process (as of 03.03.2019):

No of papers:	9	Average IF per paper:	3.476
Total IF:	31.282	Average MNiSW scoring per paper:	33.9
Total MNiSW scoring:	305	Average citations per paper:	10.35
Cited (self-citations excluded):	93		

¹⁾ IF based on Clarivate Analytics Journal Citation Reports 2018

²⁾ IF based on Clarivate Analytics Journal Citation Reports/Thompson Reuter Journal Citation Reports for year of publication

³⁾ MNiSW scoring according to the list of scientific journals 26.01.2017

⁴⁾ Citations based on Web of Science (self-citations excluded)

4.3. Scientific motivation and results

4.3.1. Scientific goals

Characteristics of solid sorbents and selection of conditions for the isolation and preconcentration of metal ions. Mechanization and automation of the process for practical applications in environmental analysis, the production and quality control of radiopharmaceuticals.

4.3.2. Introduction

The beginnings of solid phase extraction (SPE) applications for isolation and preconcentration of metal ions are associated with the isolation of lanthanides from process water samples of nuclear reactors in the early 1940s. However, due to a simple ion exchange mechanism, the method was not selective, which was a serious disadvantage in most applications. The incorporation of functional groups in the structure of sorbents forming complexes with metal ions resulted in a greater differentiation of the affinity to metal ions [1]. Therefore, the appearance of a isolation method that has solved two important problems of the analytical procedure: the effective isolation of the analyzed substance from the matrix and the possibility of simultaneous preconcentration - resulted in the intensive development of selective sorbents applications. That significantly increased the analytical capabilities of methods routinely used in laboratories, giving another impulse for the trace and speciation analysis, as well as expanded the offer of selective sorbents, particularly useful in environmental analysis. At the same time, due to the availability of materials with dedicated properties, it has become possible to modify the many analytical strategies and isolation procedures used so far to increase their efficiency and improve quality parameters. One of such areas became radiochemistry, because the growing interest in the use of radioactive substances in diagnostics and therapy has increased the demand for isotope isolation methods from a significant excess of matrix material, combined with the possibility of mechanization of procedures and connection with dedicated, automated systems for synthesis.

The results of research presented in the monothematic series of publications [H1-H9] include the results of work on the synthesis and properties of selective sorbents, applications in environmental analysis in combination with detection by spectroscopic methods, mechanization of procedures using solid phase extraction and isolation and determination of isotopes for medical diagnosis.

4.3.3. Modified sorbents

Due to the method of modification, three basic types of sorbents showing selective adsorption of metal ions can be distinguished:

- chemically modified, in which functional groups are permanently incorporated into the sorbent structure, most often with a covalent bond,
- physicochemically modified, where the compound containing functional groups is immobilized on a conventional sorbent matrix in the ion exchange or sorption process,
- ion imprinted polymers, synthesized in the presence of a template, resulting in geometrically and chemically selective structures recognizing targeted ions.

For chemical modification, the most common reaction is to incorporate an active group into the polymeric structure or silica gel matrix, to which the ligand is covalently bonded.

Physicochemical modification uses the interaction between the solid phase and the organic ligand, based on ion exchange or π^* - π interactions, leading to the immobilization of ligand molecules in the sorbent. As stationary phase, polymer ion exchangers and non-ionic sorbents are most often used.

Depending on the eluent used and the requirements of the detection technique used, the analyte can be eluted from the solid phase in the form of:

- metal ions, if an eluent is used to break the coordination bond between the modifier and the metal ion,
- metal-eluent complex, if complexing agent with higher stability constant is used as the eluent,
- metal-modifier complex, if the eluent has the ability to reduce the interactions between the sorbent and the modifier.

Modifiers are usually chemical compounds, used in other branches of analytical chemistry as chromophore or masking reagents. The desired properties of the modifier are the ability to form selective complexes with metal ions or interferences, a structure based on an aromatic system that allows to benefit from van der Waals interactions with solid phase aromatic systems and - when using ion exchangers as a solid phase - the presence of groups with high ion-exchange affinity.

A separate group are materials known as "new", "advanced" or "functional", which include carbon nanotubes (CNTs, carbon nanotubes), graphene, organometallic networks (MOFs, metalorganic frameworks) or metal oxides in the form of nanoparticles, with particular role of magnetic nanoparticles (MNPs) [2], and hybrid materials created by combining different classes of functional materials [3].

4.3.4. SPE methodology

The solid phase extraction of metal ions can be applied at various stages of the sample preparation procedure. Most often, solid phase extraction methods are used to concentrate analyte, remove interferents, separate and isolate individual fractions of the sample and in speciation analysis [4]. There are also new applications in sampling, related to direct on-site extraction of analyte [5] or using sorbents to preserve speciation forms of an element of interest [6]. The possibility of selective preconcentration of the analyte allows for a significant simplification of the procedure of collection, transport and storage of samples [7].

Solid phase extraction using selective sorbents is often used as a separated part of the analytical procedure, especially when the measuring device works in discrete mode. There are two ways to conduct the extraction process - as a static or in column system. In a static system, the specified amount of the modified sorbent is mechanically shaken with the sample solution, and then the sorbent is separated from the liquid phase by filtration, centrifugation or using the magnetic properties of the bed. The sorbent is further washed with a small volume of the eluent solution, the eluate is quantitatively separated and then analyzed. This method of preconcentration and isolation of metal ions is used in procedures that do not require a large number of replications and in determination of the basic properties of sorbents, as well as during the kinetic study of sorption process. In this case, it is much easier to operate a sorbent with magnetic properties, which resulted in the rapid development of sorbents based on ferromagnetic cores [8]. An alternative method based on microcolumns is relatively simple to implement in flow systems and is mainly used for chemically modified and physicochemically modified sorbents. Due to the ease of mechanization and automation of measurements, systems using microcolumns are used in environmental analysis [9] and radiochemistry [10].

4.3.5. Flow methods

Use of flow systems in combination with solid phase extraction in analytical and radiochemical applications has a number of advantages. The main ones include:

- the possibility of performing the series of operations, modifying the composition of the sample (preconcentration, isolation from the matrix, isolation of forms for speciation and fractionation),
- simplification of measurements by mechanization and automation of the procedure, shortening their time and improvement of analytical parameters (mainly precision). In

radiochemical applications, mechanization and automation reduce the time and number of manual intervention by the operator, which effectively decreases the dose received during work with radioactive isotopes,

- flexibility of the system for easy adaptation to variable applications (change of the detector, change of the analyte) and connectivity with other automatic systems (i.e. synthesis and final formulation of labeled compounds, isolation and purification of isotopes).

At the same time, the increasing importance of automated systems constructed for the needs of synthetic chemistry in flow conditions is observed, especially in radiopharmaceutical applications. This is a separate area in which the priority is given to reproducibility of physicochemical processes, optimized in terms of time and efficiency for synthesis, purification and final formulation of the product in the aseptic conditions of the manufacturing area and limited operator's participation.

The natural way of development is therefore the combination of isolation systems with synthesizers using the processed sample. The main aim of this action is to isolate and increase the concentration of the isotope used for labeling while eliminating impurities and matrix constituents.

4.3.6. Results

In [H1] I proposed a flow system for preconcentration and isolation of manganese on the physicochemical modified sorbent. As a modifier, I used tetracarboxyphenylporphyrin (TCPP, tetrakis (4-carboxyphenyl) porphyrin), a macrocyclic ligand mainly complexing divalent metal cations with an ionic diameter of 60-70 pm. It shows no or moderate affinity for group I and II cations, which are the main components of the sample matrix. In the static process, I determined the most favorable sorption conditions, while further preconcentration in the on-line system turned out to be a very good way to increase sensitivity and reduce the limit of quantification of the detection method (FAAS, flame atomic absorption spectrometry). For this purpose, I have constructed two flow systems using a physicochemical modification of the IRA904 sorbent using TCPP [H1 / Fig.1]. In the first of them the sample was mixed with the modifier in the solution, and then the complex was retained on the microcolumn. For elution the metal-ligand binding was broken in the reaction with nitric acid at a concentration of 2 mol/L and the manganese concentration was determined by the FAAS. The second solution was to apply the sample to the sorbent modified with tetrakaroxyporphyrin, followed by elution of the analyte to the detector. For the

construction I used easily available, small laboratory equipment: Ismatec MS/4 Reglo 4-channel peristaltic pump and 2 Rheodyne RH 5020 low pressure valves. Due to better analytical parameters, for further research I chose the system with the formation of the MnTCPP complex in solution, where I obtained the linearity in range of 20-120 mg/L, with the limit of quantification (3σ) 12mg/L and the precision of 2.2%, expressed as the relative standard deviation. I checked the efficiency of the developed method by analyzing the recovery of Mn (II) in tap water samples and comparing the results with the atomic absorption spectrometry with graphite furnace atomization (ETAAS, electrothermal atomic absorption spectrometry). The developed method was characterized by quantitative, stable recovery ($98.1 \pm 3.9\%$) and good agreement with the results of the reference method. I compared the analytical parameters with other SPE methods, using the enrichment factor (EF) to evaluate the efficiency of the process of analyte preconcentration in the column. It was determined as the ratio of the volume of the analyte solution flowing through the bed of the microcolumns to the volume of the eluent used or as the ratio of the slope of the calibration curves for the analyte in the eluate and the sample analyzed. For the proposed method, I obtained the value $EF = 30$ for a 15 mL sample. Compared with work [11], in which modified sorbent Amberlite XAD-16 1,3-diethyl-3-aminopropane-1-ol, where $EF = 300$ was achieved from a 3000 mL sample, the result obtained was significantly lower. However, the efficiency of the preconcentration process depends on the volume of the sample being concentrated or the duration of the process; a longer flow of solution passing through the sorbent bed allows to achieve higher values of EF, but at the same time significantly reduces the throughput of the analytical procedure, which is not included in the EF coefficient structure and results in the lack of consistent methodology for an objective comparison of the methods used.

Therefore, for a comparison of the flow systems performance other parameters are introduced, taking into account more factors affecting the final efficiency of the process. These include: concentration efficiency (CE), defined as the product of the concentration factor and the number of processed samples per unit of time or the consumptive index (CI), specifying the sample volume necessary to obtain a unit concentration value. Using the proposed parameters, for preconcentrating Mn (II) on a TCPP modified sorbent, I obtained CE values = 5/min and CI = 2 mL, while in the compared method [11] CE was 2.5/min and CI = 10 mL. This indicates a higher efficiency of the preconcentration process and a significant improvement in the analytical parameters of manganese determination by flame atomic absorption spectrometry in the system proposed in [H1].

An attempt to set the methodology related to the comparison of the efficiency of preconcentration and isolation methods in flow systems was made in [H2]. As an analyte for comparison, I chose cadmium, due to its high importance in the analysis of environmental samples and in the assessment of occupational exposure.

A wide range of determination methods, including: atomic flame atomic spectrometry (FAAS) or graphite furnace (ETAAS), inductively coupled plasma optical spectrometry (ICP OES) or inductively coupled plasma mass spectrometry (ICP MS), allowed to identify specific requirements for isolation and preconcentration procedures by each of these methods. Due to the higher limits of quantification for FAAS and ICP OES, it is rarely possible to determine cadmium directly, therefore the main criterion for selecting and optimizing the sample preparation method was to obtain a significant analyte concentration. The other techniques offer sufficient ranges of applicability, however, for the ETAAS the problem is high and variable salt concentrations and the presence of organic components requiring extended pyrolysis of the sample, which increases the risk of losing the analyte at this stage due to the high volatility of cadmium. These difficulties can be removed by using averaged methods of background correction or chemical modifiers, however, in this case, the corrosion of graphite elements and the rising blank should be considered [12]. Also in the case of the ICP MS, high salt concentrations and the content of organic substances adversely affect the quality of the analysis results, mainly by generating isobaric interference with the m/z values of analytes [13]. Performance analysis of the isolation and isolation methods coupled with detection techniques [H2 / tab.1,2,3], allowed to define the rules for effective coupling of the isolation technique with the detector used (Fig.1). Analysis of the obtained values of CE and CI parameters by analytical techniques confirms that in the case of FAAS, the highest values of concentration coefficients were achieved, which was necessary due to the relatively high detection limits of this method, with the simultaneous high throughput of the analytical procedure. The averaged results were: 21.4/min for the CE with the analysis of 26.7 samples per hour. The results indicate efficient coupling of flow methods with the FAAS due to the effective chemical mechanisms involved, which is confirmed by the low values of the CI. Among the cited works, the paper [14], of which I was a co-author, was placed among the best chemically optimized methods, with the CI value of 0.06 mL. Detailed values for the CE and CI calculations are provided in the tables [H2 / tab.1, tab.2, tab.3] but due large amount of the data, were not included here.

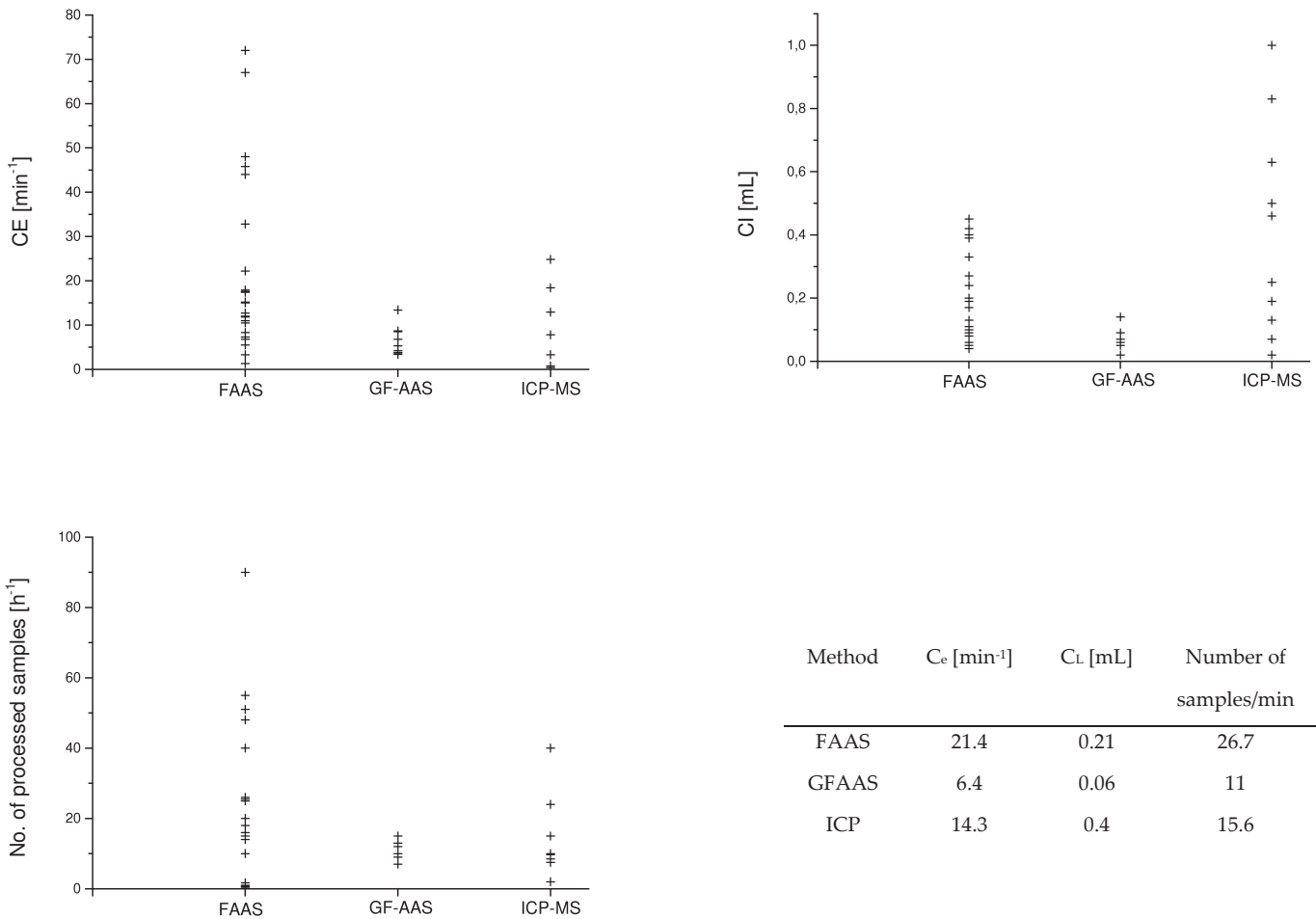


Fig.1. Parameters of preconcentration systems for the analytical techniques studied. Based on [H2].

Analyzing the performance of other mentioned techniques, it can be noticed that for GFAAS, the preconcentration is not critical, due to the sufficient application range of the method. Anyway good EF and CE are obtained, which results from a small elution volume (usually below 100 μL), especially in column-in-tip solutions [H2/Fig.2]. The system has limited throughput, which results from the sequential operating mode of the device, although this inconvenience may be partially limited by the parallel pyrolysis and atomization of the analyzed sample with the subsequent preconcentration of next sample. The results for the ICP techniques indicate, that in this case the main aim of the sample pretreatment is to reduce the concentration of matrix components.

Comparing properties of sorbents used, two new trends could be observed. The first is the growing role of new materials, different in properties from the standard styrene-divinylbenzene polymers (PSDVB) such as nanomaterials or polymers, especially these with ion or molecular recognition. The second one is the use of non-conventional methods of immobilizing the stationary phase - interesting analytical and flow parameters were obtained with knotted reactors [H2/tab.4]. These observations became the inspiration for two further works: [H3] and [H4], which used as a sorbent a polymer selective for copper ions, applied as a stationary phase in knotted reactor.

One of the methods of obtaining chelating sorbents is the polymerization of monomers, having in their structure groups forming complex with metal ions. I used this concept in [H3] for synthesis of conductive polymer 1,8-diaminonaphthalene (1,8-DAN) as a sorbent, due to its affinity for some metal ions in electrochemical experiments [15]. However, the thin layers obtained for these purposes did not provide sufficient sorption capacity in the solid phase extraction technique. Thus I checked two strategies to obtain poly-1,8-diaminonaphthalene by direct polymerization, which involves the oxidation of the monomer with iron (III) chloride or ammonium persulfate. For both materials essential characteristics have been measured such as specific surface area, micropore volume, pore size and chemical composition.

In the scanning microscope study a varied morphology in both polymers was observed. Monomer oxidized with FeCl_3 had an irregular structure, while in the case of oxidation with $(\text{NH}_4)_2\text{S}_2\text{O}_8$, the polymer grains were spherical. I compared the affinity of both sorbents and observed significant differences in the sorption efficiency of metal ions. Effective preconcentration of metal ions: Mn, Cd, Zn, Cu, Ni, Co and Pb showed polymer synthesized with FeCl_3 . An interesting property had a second polymer, as it showed a high selectivity for copper ions, allowing almost quantitative sorption of these ions, with a high sorption capacity, determined at 23 mg/g, exceeding significantly the results obtained for traditional PSDVB sorbents [16-17]. Favorable sorbent characteristics were used for the construction of a flow system, based on a knotted reactor, for the selective preconcentration of Cu (II), presented in the article [H4]. I compared the affinity to some metal ions to poly-1,8-diaminonaphthalene, obtained by polymerisation with $(\text{NH}_4)_2\text{S}_2\text{O}_8$ with the Chelex-100, sorbent with the diiminoacetic groups, commonly used for the isolation.

In the design of the flow system, I used the knotted reactor instead of the typically used column. To immobilize the polymer, I proposed a new concept, partially using a scheme known for physicochemical modification of sorbents by applying a monomer layer to the inner surface of the Teflon capillary, followed by polymerisation in the oxidant stream. The

selectivity coefficients of the setup for other metal ions versus Cu (II) at pH 3 were: 20 for nickel, 35 for manganese, 49 for cadmium and 198 for zinc.

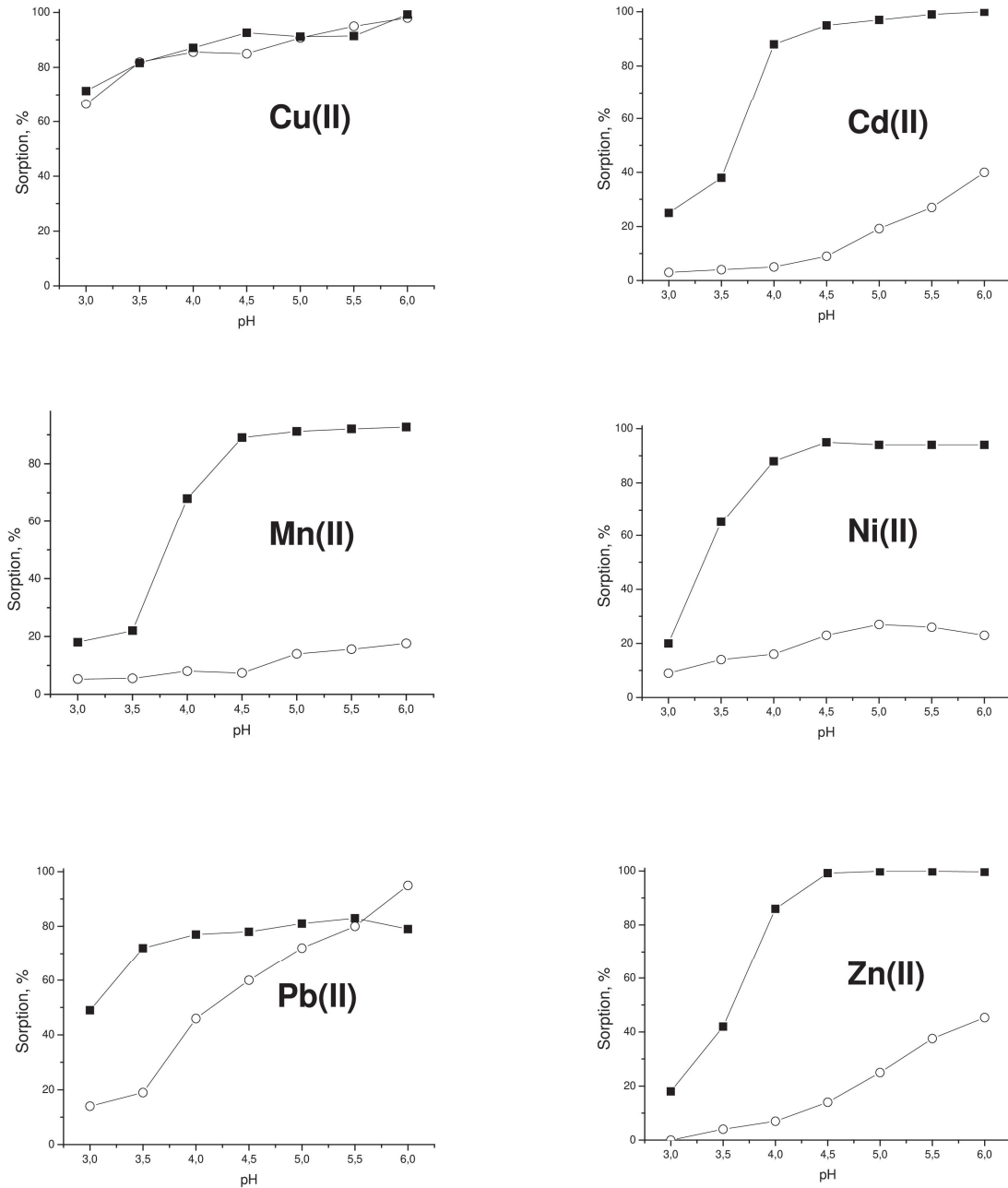


Fig.2. Metal ion sorption profiles for 1,8-DAN (O) and Chelex-100 (■) [H4]

I also examined the mechanism controlling the speed of the sorption process by analyzing the agreement of experimental data with different models of sorption kinetics and determined the

diffusion in the sorbent structure as the dominant mechanism in the sorption process. Based on experiments in the dynamic system, I determined pH 3.5 as the optimal for Cu (II) preconcentration at 1.4 mL/min sample flow and the quantitative elution was achieved using 0.5 mL nitric acid solution. With the FAAS detection it was possible to accurately and precisely determine the concentration of copper ions in groundwater.

The sorption of metal ions at much lower concentration levels was investigated using gamma spectrometry as the detection method. The proton cyclotron operated in the Center for Production and Research of Radiopharmaceuticals at the University of Warsaw, was used for irradiation of samples and analytical techniques similar to the method of neutron activation analysis were used for the measurements of delayed gamma radiation. In this case, however, nuclear reactions are induced mainly with a 16.5 MeV proton beam and partly with secondary neutrons.

The subject of work [H5] was the distribution of metallic impurities and radiometals in the production process of radiopharmaceutical ^{18}F -fluoro-2-deoxyglucose, described in detail in [18], which I was a co-author. For the tests I chose the following elements of the synthesis system: Accel Plus QMA ion exchange column used to preconcentrate and isolate fluorine-18 (^{18}F) from the target material, SepPack C18RP reversed phase SPE column used for basic hydrolysis and product purification and Seppack NPlus aluminum oxide column to remove ionic impurities. With a high-resolution gamma spectrometer equipped with germanium detector (HPGe) I analyzed radionuclides in the final product, the saline used for the final formulation, liquid waste after synthesis and recovered target material. I identified fifteen isotopes that were fluorine-18 (^{18}F) contaminants.

In most cases these isotopes originated from the target body or target construction elements, resulting from the interaction with secondary neutrons in reactions (n, p), (n, α) and (n, γ) and by direct irradiation with a proton beam. The largest contribution in the total activity of radionuclidic impurities had ^{56}Co , ^{57}Co , ^{58}Co cobalt isotopes, were present mainly in the recovered target material. Rhenium and technetium isotopes, mainly as $^{183}\text{ReO}_4^-$ and $^{95,95\text{m}}\text{TcO}_4^-$, were captured by the anion exchange column and were the main radionuclidic contaminants retained on the QMA column. The qualitative analysis of the identified radionuclides was in line with predictions, based on possible side reactions with construction materials. In quantitative measurements, it was critical to determine the content of impurities in the finished product, due to the potential hazard in clinical applications. In this case, the activity of contaminants, mainly ^{52}Mn and ^{56}Co , did not exceed $10^{-8}\%$ and was below the limits set in the European Pharmacopoeia [19].

For the determination of metallic impurities I used the ICPMS technique and analyzed, using the same methodology as radiometallic impurities, concentrations of Ag, Al, Cd, Co, Cr, Cu, Mn, Mo, Ni, Pb, Ti, V and Zn, which may have been distributed in the technological process. Metallic impurities were analyzed in liquid samples taken from the system and after elution of the columns used in the synthesis with 1 mL aliquot of 1 mol/L HNO₃. The sources of contamination are Havar® foil and stainless steel elements which contacted target material during irradiation and transport to the synthesizer. Observed increased concentration of lead results from the common presence of shielding materials in the process of irradiation, transport and production of a radiopharmaceutical. In the final product the increased concentration of nickel is observed, resulting from the final formulation process, carried out with disposable metal needles. In summary, concentrations of radioisotopic and metallic pollutants are much lower than the limits [19] and do not pose a threat in clinical applications. The subject of further research, combining radiochemistry with metal ion isolation methods, were papers [H6] and [H7] on new sorbents for the isolation of metal ions. I investigated the carbon sorbents for isolation the scandium from solutions with a very high content of matrix elements. The long-term goal was to develop effective methods for isolation of scandium radioisotopes from solutions with very large excess of calcium ions. Carbon sorbents are very often used in the process of isolation and preconcentration of metal ions due to the very well developed porous structure, large specific surface area and the presence of additional functional groups. In [H6] I used carbon-based sorbents, such as activated carbon and carbon nanotubes, modified with carboxyl groups and graphene oxide. The oxidation of their surfaces improves the hydrophilicity and increases the number of functional groups containing oxygen atoms, such as carboxyl-, hydroxyl- or ketone groups, improving sorption. Based on the analysis of microscopic images and pore sizes, activated carbon was classified to microporous sorbents with a large specific surface area (400 m²/g), while the other had less micropores and lower specific surface areas (175-220 m²/g) but with greater number of surface acidic groups (2.4-3.2 mmol/g, determined by the Boehm method).

The sorption of scandium ions increases with increasing pH on all materials studied. This is due to the increase in negative charges on the surface of the sorbent, which interacts with metal cations. Sorption of Sc (III) on carbon nanotubes and graphene oxide is practically quantitative in the pH range 2.5-5.5, and in the case of graphene oxide the effective sorption is observed even at pH 1 (about 80%). Activated carbon is characterized by a significantly lower sorption (Fig. 3A).

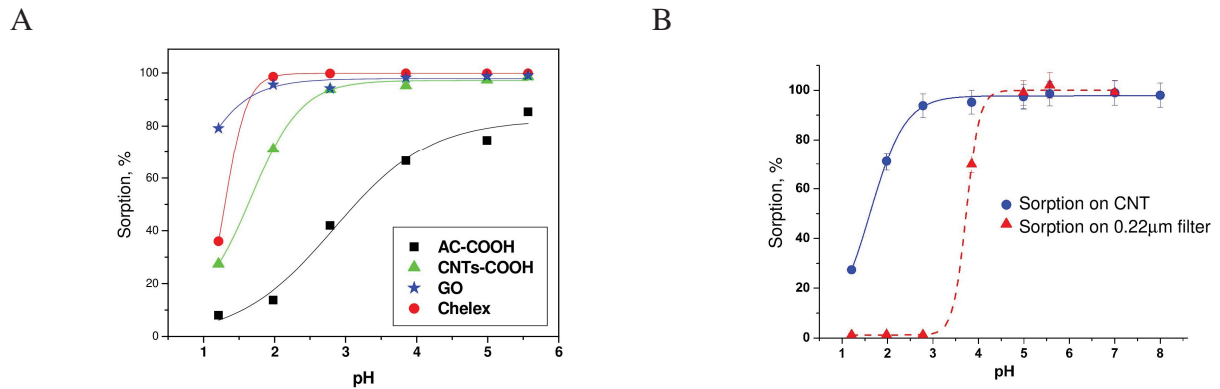


Fig.3 Influence of pH on the sorption of scandium ions (III) on carbon sorbents (A) and on 0.22 mm filter (B). Based on [H6, H7]

This proves the dominance of the effect resulting from the presence of functional groups on the surface of sorbents over the effects resulting from a large specific surface area and enables effective isolation from typical matrix components (Na, K, Ca, Mg ions). This property is particularly valuable for scandium isolation, because at a relatively low pH (about 4.0 for a low ionic strength of the solution and in the absence of agents complexing scandium, Fig 3.B) the $\text{Sc}(\text{OH})_3$ is formed and mechanical deposition of hydroxide on the bed surface in the filtration process occurs.

Under the proposed conditions in [H6], the scandium was stable in a solution up to pH 5.5, which I checked in a test on a 0.22 μm pore size filter. At pH above 5.5, I observed an increase in the retention of Sc (III) on all sorbents as a result of mechanical sorption, which was confirmed experimentally in [H7] and [H9]. The possibility of formation of insoluble scandium was not taken into account by the authors of other papers investigating the sorption of scandium at a neutral pH [20-22], which may lead to an overestimated sorption capacity of the sorbents they studied. Another favorable characteristic of graphene oxide was the high sorption capacity for scandium at low pH, reaching 36.5 mg/g sorbent, about 20 times higher than for the reference sorbent Chelex-100, also exceeding the performance of other sorbents proposed in the literature [20,21,23]. I have shown that carbon nanomaterials can be effective sorbents for scandium, showing a significant advantage in lower pH over the routinely used Chelex-100.

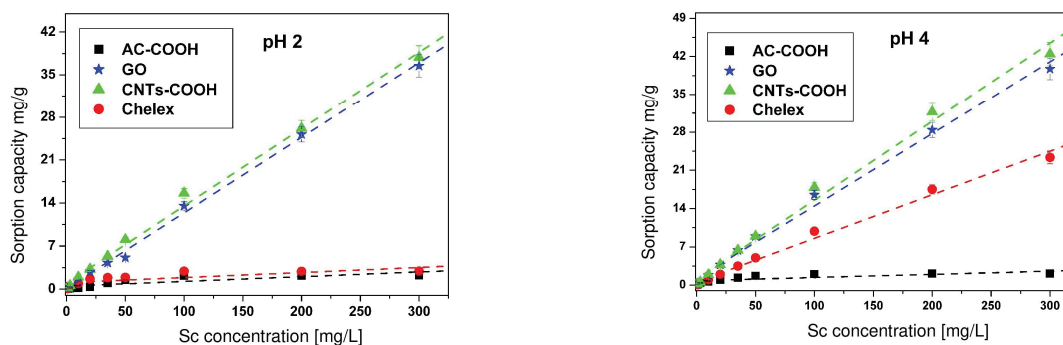


Fig. 4 Effect of Sc (III) concentration on the sorption capacity of sorbents at pH 2 and pH 4. Based on [H6]

I used the advantages of carbon sorbents in [H7], for isolation of Sc (III) in the presence of a significant excess of calcium ions, for further applications in radiochemistry. This was related to the growing interest in scandium radioisotopes, due to the potential applications in diagnostics and therapy. Production in cyclotrons by irradiation of calcium targets caused the need to develop effective methods of isolation sub-ng amounts of scandium from the target material. Although calcium is not toxic and can be present in pharmaceutical preparations, its excess significantly reduces the labeling yield with radioisotopes and must be effectively eliminated. For scandium isolation in low pH I used carbon nanotubes packed in the microcolumn in a flow system, seeing that the scandium as a Sc^{3+} cation occurs in a relatively narrow pH range and, with increasing pH, rapidly form the insoluble $\text{Sc}(\text{OH})_3$, with narrow pH range for $\text{Sc}(\text{OH})_2^+$ and $\text{Sc}(\text{OH})^{2+}$ occurrence. Therefore, due to the possible formation of weak or insoluble forms of scandium at higher pH (> 4), I checked the mechanical sorption using a $0.2 \mu\text{m}$ filter. Carbon nanotubes showed effective sorption of scandium ions already at pH 2, while for $\text{pH} > 4$, I observed an increasing mechanical deposition, confirmed by the quantitative deposition of scandium on the filter surface. This allowed to confirm the hypothesis from the paper [H6], given to the works [20-22], and regarding mechanical filtration as the dominant mechanism of scandium uptake at pH above 4, not related to the sorption properties of the materials used. Due to the purpose of the work, I paid particular attention to the effective removal of calcium ions from the solution. I examined the effectiveness of calcium washing with 0.01 mol/L HCl solution and I found that 15 mL of this solution removed the excess Ca (II) without losses of Sc (III) on the column. I also checked

the analytical parameters of the method and the applicability as a designed system for scandium determination in environmental samples [H7/tab.2]. Due to good parameters of scandium isolation on carbon materials, I checked the possibility of scandium isolation on graphene oxide and nanotubes modified with carboxylic groups in simulated scandium-44 production. For both carbon sorbents, I observed efficient sorption in the assumed pH range, a very high sorption capacity and a significant reduction in the amount of calcium in the eluate. However, after the tests in the flow system, I gave up further work with carbon materials due to the strong compression of the bed, which resulted in a large increase in flow resistance in the system and hamper the mechanization and automation of the isolation process.

Therefore, in the review [H8], I analyzed the methods of isolation and preconcentration of Sc (III) in various applications - from large-scale industrial to medical, to develop the optimal ^{44}Sc isolation route in the automatic system. Radiochemical applications were dominated by precipitation methods or using dedicated resins for actinides and trivalent rare earth metals. In the first case, the limitation was co-precipitation of contaminants and high variability of precipitation conditions, in the second a considerable volume of the eluent used and the necessity of using a two-stage procedure with subsequent preconcentration on cation exchanger. Both inconveniences may hinder or complicate the process automation. Thus the integration of several concepts from various areas of research and technology was crucial for the effective isolation of scandium. In work [23], high selectivity of sorbents based on carboxylic groups at low pH was found for isolation of scandium from post-process effluents in the processing of bauxite. Other point was the selection of the methods used in environmental chemistry, in which chelating sorbents were used to isolate and preconcentrate the scandium ions, indicating quite high selectivity of diiminoacetic groups for the scandium in complex matrix [24]. Liquid extraction methods using extractants containing carboxylic groups [25] showed differences in optimal sorption conditions between scandium and other rare earth metals. Compiling the above conclusions, I decided to check the hypothesis that the optimal way to isolate the scandium in terms of process automation would be the use of a chelating sorbent with diiminoacetic and/or carboxylic groups at low pH.

In [H9] I combined observations related to the automation of scandium isolation processes with the selection of a sorbent with appropriate properties. The reason was the increase in the application of scandium-44 isotope for the medical diagnosis. One of the promising methods of production is the irradiation with a proton beam the calcium carbonate enriched with the calcium-44, and then the isolation of the isotope from the target material. As I mentioned in [H8], the so far used solutions were dominated by precipitation methods based on filtration of

the $\text{Sc}(\text{OH})_3$ after alkalization of dissolved target. Further analysis indicated potential weaknesses in the scandium isolation as a precipitate from the alkaline environment. I observed significant variability in isolation efficiency due to: narrow and variable range of optimal pH of precipitation reaction, high dependence of concentration and elution efficiency from the time of contact of solutions with filter and strong increase of backpressure on the filter resulting from the presence of graphite suspension in solution. This allowed the scandium to be separated by classical laboratory methods, but it significantly impeded the use of this method for automation.

I tried to solve this problem and as a sorbent for extraction of scandium ions I chose Nobias sorbent, characterized by very high affinity to metals, and especially to rare earth metals, with very limited sorption of ions considered as matrix like Ca, Mg or alkali metals. The sorbent was selected based on the review of methods for determining scandium in environmental samples [H8], thanks to a particularly advantageous set of properties: Nobias has very low affinity for alkali metals [26] combined with quantitative sorption of transition metals at pH 5-6 [27], significantly decreasing at about pH 4 [28-29]. Sorption of rare earth metals in the pH range 4-6 is equally effective [30-31]. Considering the observation indicated in [H8], regarding effective sorption of scandium in lower pH than for rare earth elements, I investigated the sorption of pH in the range of pH 3-10, obtaining practically quantitative sorption already at pH 3 [Fig.1/H9]. An additional advantage was the poor sorption of calcium ions under these conditions, enabling direct recovery of the calcium-44 isotope from the effluent, which is economically advantageous due to the high cost of the calcium carbonate-44 ($^{44}\text{CaCO}_3$).

An important parameter of the radiochemical isolation process, in addition to efficient isolation, is to obtain high chemical purity of the eluate. For Nobias the chemical purity was clearly better compared to other works using either sorbents for solid phase extraction or filtration methods [H9/tab.1]. Another advantage of the proposed system was a very small volume of eluate (100 μL) after the isolation process. It results in the high final specific activity of the obtained scandium isotope, which increases the efficiency of labeling.

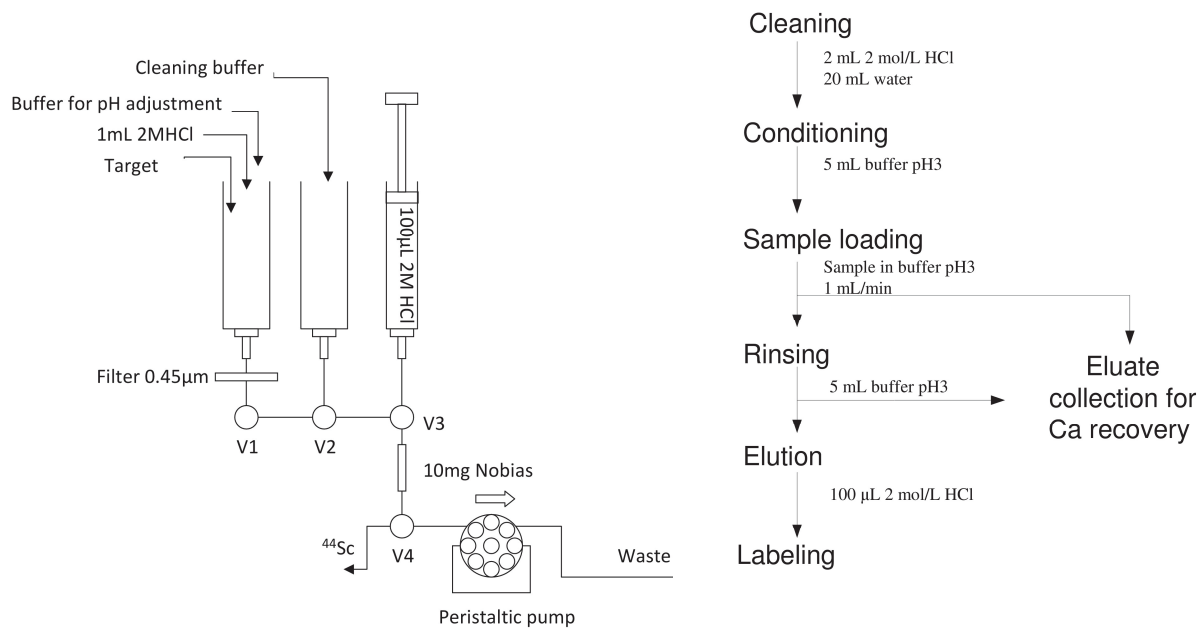


Fig.5. Scheme of the system to isolate scandium from calcium targets and the sequence of operations. Based on [H9].

The process of scandium isolation was automated in a system that was based on a standard three valves unit, controlled by commercially available modules for radiochemical synthesis, which allows the system to be incorporated into the synthesis path. The designed system used a multi-channel peristaltic pump to transport solutions. Only for column elution, to reduce the possibility of contamination of the final eluate, I used an additional channel, supplied by a micropump, where the eluent passed only through the column, minimizing the contact of the eluate with other elements of the system, which had a positive effect on the impurities level in the eluate.

As an indirect measurement of chemical purity, I also determined the minimum amount of peptide that is necessary for quantitative reaction with the scandium-44 present in the solution. I obtained a value of 0.07 nmol, which is comparable to the results obtained after the two-stage isolation of cyclotron scandium-44 on DGA sorbent and significantly better than the results obtained for scandium-44 obtained from the $^{44}\text{Ti}/^{44}\text{Sc}$ generator [32].

Resins				
Resin	Isolation efficiency [%]	Eluent / Final volume [μ L]	Impurities [mg L ⁻¹]	Ref
DGA+Dowex 50	75	1 mol L ⁻¹ NH ₄ OAc /	Pb<0.7, Al<1, Zn<1,	[33]
DGA+SCX	93	1500 NaCl/HCl / 700	Cu<0.02	
UTEVA	80	H ₂ O / 400	N/A	[34]
Chelex 100	70	1 mol L ⁻¹ HCl / 500	N/A	[35]
DGA	88±3	0.1 mol L ⁻¹ HCl / 10000	Fe 1.14, Al 1.14	[36]
UTEVA	80±4	H ₂ O/1 mol L ⁻¹ HCl / 400	Ca 82, Fe 5.2, Zn 4.7, Ni 29, Al. 6.4, Mn 2.0	[10]
DGA+ SCX	89.7±3.1	4.8 mol L ⁻¹ NaCl + 0.13 mol L ⁻¹ HCl / 700	N/A	[37]
Nobias	94.9±2.8	2 mol L ⁻¹ HCl / 100	Al 0.009, Ca 0.34, Cu 0.02, Fe 0.005, Mn 0.014, Ni 0.013, Pb 0.03, Zn 0.03	[H9]
Filtration				
Filter	Isolation efficiency [%]	Eluent / Final volume [μ L]	Impurities [mg/L]	Ref
0.22 μ m filter	96	0.5 mol L ⁻¹ HCl / N/a	Ca<1, Fe 0.07	[38]
0.22 μ m filter	93.6±3.9	6 mol L ⁻¹ HCl / 3000	N/A	[39]

Table 1. Comparison of scandium isolation methods. Based on [H9]

The designed system has been attached to the standard commercially available Eckert-Ziegler TracePharm system enabling full automatic isolation of the isotope and final synthesis of the scandium-44 labeled peptide. The developed methodology of isolation of ⁴⁴Sc and further synthesis was used for preclinical studies of the ⁴⁴Sc-DOTATATE peptide as a diagnostic radiopharmaceutical in the detection of neuroendocrine tumors.

4.3.7. Summary

In the above-mentioned publication cycle, I presented the results of studies on static and flow methods for isolation and preconcentration of metal ions. The most important are:

1. demonstration that physicochemical modification of sorbents can be an easy and effective way to impart desirable sorption properties, as evidenced by the results of Mn preconcentration on a sorbent modified with tetracarboxyphenylporphyrin [H1] and analysis of flow system parameters using different extraction modes to the solid phase [H2],
2. synthesis and assessment of sorption properties of 1,8-diaminonaphthalene polymer and demonstration of copper selectivity for polymer synthesized in the presence of ammonium persulphate [H3] and construction of flow system for copper determination using polymer surface modification of knotted reactor [H4],
3. determination of distribution and quantitative assessment of metallic and radiometallic impurities in the production process of the FDG radiopharmaceutical [H5],
4. the use of carbonate nanosorbents (graphene oxide, carbon nanotubes) for sorption Sc (III), obtaining effective and selective vs. Ca sorption at low pH. At the same time, I showed that the results obtained at pH close to neutral, presented in some works, they are burdened with methodological errors related to the precipitation of the scandium hydroxide and an exaggerated assessment of sorption properties [H6-8],
5. selection a tailored sorbent, properties assessment and development of flow system for automated isolation of the ^{44}Sc radioisotope [H8-9].

4.3.8. Bibliometric summary

The results of the research presented as a series of publications "Static and flow methods for the isolation of metal ions on solid sorbents - analytical and radiochemical applications" are research results published in 9 papers in journals indexed in the JCR database. The results are the effects of work in small research groups in which I played a leading or significant role: in 4 papers I was the first author, in 5 the second with contribution no less than 40%.

In six papers I was a corresponding author. None of the presented works is a work published as post-conference materials. IF values were presented in accordance with the publication year. For publications published in 2017, 2018 the IF was given for 2017. The total impact factor of the works is 31.282.

The MNiSW scoring was prepared in accordance with the current unified list of scientific journals published for the year of publication. For the latest publications, the most current available data was adopted. The sum of points for the publication cycle is 305.

4.3.9. Perspectives

The intensive development of techniques for determination of metal concentrations and the increasing availability of equipment allowing for routine analysis of metals in environmental samples at the level of ng/g and lower, reduced the need for basic application of SPE, which was the lowering the determination limit.

Due to the growing interest in diagnostics and therapy with the use of metallic isotopes and the intensive development of isotope producing infrastructure (system of solid target irradiation in ŚLJCJ, system for the production of metallic isotopes at Voxel in Krakow, designed CERAD center in NCBJ in Świerk) an increase of interest in effective and easy to automate isolation methods is expected. The isolation and preconcentration methods currently used in radiochemistry are mainly based on ion exchange and do not fully exploit the potential of new SPE materials. My further research and scientific plans are related to the development and automation of the methods of isolation of metallic radioisotopes obtained in cyclotrons and integration with systems for automated synthesis of radiopharmaceuticals.

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4.4. Other scientific interests and research achievements

In the years 1993-1998 I studied at the Interfaculty Studies of Environmental Protection at the University of Warsaw, which I graduated with honors. Master's thesis "Leszcz (Abramis brama L.) as a biomonitoring species in the Polish Environmental Specimen Bank" I prepared in the Laboratory of Applied Analytical Chemistry of the Faculty of Chemistry University of Warsaw, under the supervision of prof. dr. hab. Jerzy Golimowski. The results of the research were presented in the publication D20 and the thesis was awarded the 1st prize by the German Foundation for Environmental Protection (DBU).

In 2000, I began doctoral studies at the Faculty of Chemistry University of Warsaw under the supervision of prof. dr hab. Krystyna Pyrzyńska. The work concerned on new analytical applications of tetracarboxyphenylporphyrin and included the characteristics of complexes with metals and possible application in sorbent modification. The results of the research were presented in 6 publications [D13-15, D17-19] and the dissertation was awarded the prize of the Committee of Analytical Chemistry of the Polish Academy of Sciences in 2005.

Since 2007, I have been involved in the design and implementation of the Radiopharmaceutical Research and Production Center at the University of Warsaw, where I was a member of the team preparing the production of radiopharmaceuticals for positron emission tomography and was responsible for setting up a quality control laboratory and organizing the production of radiopharmaceuticals labeled with fluoride-18 [D12, D15]. In

2008-2009, in a frame of a scholarship from the International Atomic Energy Agency, I completed post-graduate studies in radiochemistry and radiopharmacy at ETH in Zurich. After start-up the Center, my research interests covered the development of the manufacturing process and quality control of ^{18}F -labeled radiopharmaceuticals (^{18}F -fluorodeoxyglucose [D10, D11], ^{18}F -fluoromidazole [D1, D6]), carbon-11 (^{11}C -methionine [D5], ^{11}C -acetate [D5, D7]). The next direction of the study was the preparation of radiopharmaceuticals labeled with metal isotopes: gallium-68 [D3, D9], copper-64 [D4], scandium-43 and -44. The developed technologies allowed the introduction of diagnostic techniques using radioisotopes and Animal-PET imaging for biomedical projects (item 5H, 2-5), in cooperation with the Military Medical Institute, Institute of Experimental and Clinical Medicine and the Warsaw University of Life Sciences.

A handwritten signature in blue ink, reading "Krzysztof Kilian", written over a horizontal dotted line.