

**Separation and Purification of ^{111}In from Irradiated
Cadmium Targets by Solid Phase Extraction (SPE)
Method for Medical Applications**

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To my life inspiration

My sons

Idin and Samad

1	Introduction	4
1.1	Background.....	4
1.2	Medical uses of radioisotopes.....	4
1.3	Radioisotope production	5
1.4	Diagnostic radionuclides	6
1.5	Therapeutic radionuclides	6
1.6	In-radioisotopes in different research.....	8
1.7	¹¹¹ In production methods	10
1.8	¹¹¹ In characteristics and medical applications.....	16
1.9	¹¹¹ In separation and purification methods	17
1.9.1	Liquid–Liquid Extraction.....	18
1.9.2	Solid Phase Extraction (SPE)	19
1.10	Aim of this work.....	20
2	Counting techniques	21
2.1	Radiometry.....	21
2.1.1	Counting beta and electron emitters	22
2.1.2	Counting electron capture.....	22
2.2	Principle of LSC	22
2.2.1	Scintillation counting component	23
2.2.2	Photomultiplier	24
2.2.3	Energy transfer in liquid scintillation solutions.....	24
2.2.4	Energy transfer between solvent molecules	27
2.2.5	Solvent molecule-scintillator Energy transfer	27
2.2.6	Fluorescence	28
2.3	Background.....	29
2.3.1	Luminescence effect.....	31
2.3.1.1	Chemoluminescence.....	31
2.3.1.2	Photoluminescence.....	31
2.4	Quench effect.....	32
2.4.1	Electron capture (photon quenching).....	33
2.4.2	Color quenching.....	33
2.4.3	Concentration quenching	33
2.4.4	Chemical quenching	33
2.4.5	Phase quenching	34
2.5	Quench correction methods.....	34
2.5.1	Internal standard method	35
2.5.2	Sample Channels Ratio (Non-standard method).....	35
2.5.3	External standard.....	36
2.6	Pulse Shape Discrimination	37
2.7	Structure of the measuring systems.....	38
2.7.1	LKB Wallac 1220 Quantulus	39
2.7.1.1	Shielding	40
2.7.2	Tri-Carb liquid scintillation system	40
2.8	Calibration curve and efficiency	41
2.9	Gamma spectrometry	43
3	Experimental	45
3.1	Materials and Methods.....	45
3.1.1	Reagents	45
3.1.2	Devices.....	46
3.2	Solid Phase Extraction materials	47

3.2.1	TEVA Resin®.....	47
3.2.2	Organophosphorus chelating agents	49
3.2.2.1	Actinide Resin®	49
3.2.2.2	Ln Resin®	51
3.2.2.3	TRU Resin®.....	52
3.3	Separation Procedures and Methods.....	54
3.3.1	Determination of weight distribution (D_w) and decontamination factors-- (D_f).....	55
3.3.1.1	Sample preparation.....	56
3.3.1.2	Counting and calculations	58
3.3.2	Elution study	60
3.3.3	Column characteristics and preparation.....	60
3.3.4	TEVA Resin® experiments	61
3.3.4.1	TEVA Disc experiment	62
3.3.4.2	The reuse of one TEVA Disc®	62
3.3.5	TRU, Actinide and Ln resins experiments.....	63
3.3.5.1	Elution study for Ln Resin® and Ac Resin®.....	63
3.3.6	Influence of inactive Cadmium in separation	64
3.3.6.1	D_w determination	65
3.3.6.1.1	Sample preparation and procedure	65
3.3.6.2	Elution studies.....	65
3.3.6.2.1	Sample preparation and procedure	66
3.3.6.2.2	^{109}Cd decontamination factor (D_f).....	67
3.3.7	Possibility to reuse of one column	67
3.3.8	Extraction of several inactive metal traces.....	67
3.3.8.1	Metal trace analysis by ICP-OES	68
3.3.8.1.1	Sample preparation and procedure	68
3.3.9	Final indium recovery (extraction).....	70
3.3.9.1	Sample preparation and procedure.....	70
3.3.10	Simulated experiment	71
3.3.10.1	Sample preparation and procedures.....	71
3.3.10.1.1	Separation steps	71
3.4	^{109}Cd Recovery	73
3.4.1	Evaluation of D_w values	74
3.4.1.1	D_w values experiments (TEVA Resin® water and HCl pH5)	74
3.4.1.1.1	Sample preparation	74
3.4.2	Elution study (TEVA prepacked columns).....	75
3.4.3	TEVA Resin®, ^{111}In extraction and ^{109}Cd recovery	75
3.4.3.1	Sample preparation (without adding any impurities)	76
3.4.3.2	Influence of metal impurities and inactive Cd on TEVA Resin®..	76
3.4.3.2.1	Sample preparation and procedures	77
3.4.3.2.2	Determination of metal impurities via “Atomic Absorption”	77
3.4.3.3	Possibility to re use the TEVA column	78
3.5	Real target experiment.....	78
3.5.1	General description of CV-28 Cyclotron.....	79
3.5.1.1	Irradiation condition.....	79
3.5.2	Targetry	80
3.5.2.1	Target material	80
3.5.2.2	Irradiation test	80
3.5.2.3	Irradiation for separation experiments.....	80
3.5.3	Preparation of real sample solution	81

a)	Solution 1.....	81
b)	Solution 2.....	81
c)	Solution 3.....	81
3.5.4	Activity detection.....	81
3.5.5	Separations.....	82
3.5.5.1	Separation procedure.....	82
4	Results and discussion.....	83
4.1	D _w values, TEVA Resin®.....	83
4.1.1	Elution behavior of ¹¹¹ In and ¹⁰⁹ Cd on TEVA® Disc.....	87
4.1.1.1	Reuse of TEVA® Discs.....	89
4.1.2	EDTA D _w values.....	90
4.2	D _w values Ac Resin®, Ln Resin® and TRU Resin®.....	91
4.2.1	Ln Resin®, HNO ₃ and HCl.....	92
4.2.2	Ac Resin® HCl, HNO ₃	94
4.2.3	TRU Resin® HCl, HNO ₃	96
4.3	Elution behavior of ¹¹¹ In and ¹⁰⁹ Cd on Ln and Ac resins.....	97
4.4	Influence of stable Cd, Fe, Al and Cu.....	99
4.4.1	Influence of macro amounts of stable Cd on ¹¹¹ In recovery.....	100
4.4.1.1	In D _w values.....	100
4.4.1.2	Elution study (In recovery and decontamination factors).....	101
4.4.1.3	Reuse of Ln and/or Ac Resin.....	104
4.4.2	Influence of trace metal impurities and stable Cd.....	105
4.4.2.1	Metal trace standards and blank calculation.....	105
4.4.2.2	Quantification of metal impurities.....	106
4.4.2.3	Yield of the ¹¹¹ In extraction.....	108
4.5	Simulated Experiment.....	109
4.5.1	¹¹¹ In Recovery.....	109
4.5.2	Cd Decontamination Factor (D _f).....	111
4.6	¹⁰⁹ Cd Recovery.....	112
4.6.1	D _w values, TEVA Resin®.....	112
4.6.2	Elution study (TEVA-prepacked columns).....	115
4.6.3	Cd Elution using EDTA-solution.....	117
4.6.4	Influence of stable contaminants on Cd recovery from TEVA column.....	118
4.6.4.1	Influence of varying amounts of stable impurities.....	119
4.6.5	¹⁰⁹ Cd recovery and ¹¹¹ In separation, TEVA column.....	121
4.6.5.1	Reuse of TEVA columns for Cd recovery.....	122
4.7	The real sample experiment.....	123
4.7.1	Irradiation of the natural cadmium.....	123
4.7.2	Radioactivity determination.....	123
4.7.3	Separation of ¹¹¹ In form real natural Cd targets by SPE method (TEVA, Ac and Ln resins).....	125
4.7.3.1	Real target separation via Ac and Ln columns.....	126
4.7.3.2	Radioisotope impurity detection by gamma spectroscopy.....	128
4.7.3.3	Real target separation via TEVA Resin®.....	130
5	Conclusion.....	133
6	References.....	139

1 Introduction

1.1 Background

Dedicated radiochemicals with high specific activity are very useful to solve some problems in nuclear physics, nuclear chemistry and nuclear medicine. In recent years, a variety of methods have been described in order to optimize the necessary radiochemical separations. Modern radiochemical methods allow to produce rather pure radioisotopes /Fil01/. Over the last thirty years the use of radiopharmaceuticals in nuclear medical procedures have become standard for non-invasive diagnosis of cancer /Wei03/. The use of radioisotopes in the field of nuclear medicine is the most impressive and socially useful spin-off of nuclear science. With radiochemicals and radiopharmaceuticals becoming more useful in medicine, companies are striving to develop and manufacture the needed compounds in order to supply the large demand /Gel04/Cho01/.

1.2 Medical uses of radioisotopes

Medical uses of radioisotopes, radiochemicals and radiopharmaceuticals can be separated into two categories: diagnostic and therapeutic. For diagnostic applications radioisotopes of short half-lives are desired in order to limit the radiation dose to which the patient is exposed. Example are Technetium-99m, Iodine-123 or Iodine-131, Thallium-201, Indium-111, Fluor-18, and also Strontium-82 decaying to Rubidium-82. The last two are used in positron emission tomography (PET). Additionally, these isotopes need to decay in such a way that their decay products are imageable (i.e. gamma ray emitters). On top of this, the isotopes need to have decay energies less than 300 keV (typically 100 to 250 keV), thus the emitted particle may be easily detected after penetrating the body. For therapeutics applications, isotopes need to have long enough half-life and usually higher energetic (>1MeV) beta emitters, such as Palladium-103, Iodine-131 and Yttrium-90 /Gel04/Rob96/.

1.3 Radioisotope production

The radionuclides available for nuclear medicine fall in three categories:

- 1) The reactor produced radionuclides; are either produced by controlled nuclear reactions with fast and thermal neutrons or obtained as fission products. Some of these radionuclides are listed in table 1-1.
- 2) The cyclotron produced radionuclides; are prepared by nuclear reactions initiated by accelerated charged particles.
- 3) The generator produced radionuclides; are produced as short-lived daughter nuclides during the decay of longer-lived radionuclides, these parent nuclides being obtained by one of the above means.

Table 1-1: Reactor produced radionuclides

Transmutation process	Neutron type	Nuclear reaction
(n, γ)	Thermal neutrons (<0.1 eV)	$^{50}\text{Cr} (n, \gamma) ^{51}\text{Cr}$ $^{124}\text{Xe} (n, \gamma) ^{125}\text{Xe}$ $\xrightarrow{\text{EC}} ^{125}\text{I}$
(n, γ)	Fast neutrons (>1M eV)	$^{32}\text{S} (n, p) ^{32}\text{P}$ $^{59}\text{Co} (n, p) ^{59}\text{Fe}$
(n, f)	Nuclear fission	$^{235}\text{U} (n, f) ^{99}\text{Mo}$ $^{235}\text{U} (n, f) ^{131}\text{I}$

In contrast to the reactor produced radionuclides, which as a rule show an excess of neutrons, cyclotron produced radionuclides are neutron deficient isotopes. They are produced by bombarding stable isotopes with charged particles (protons, deuterons, α -particles or other light nuclei). Due to their neutron deficiency, cyclotron produced radionuclides normally decay by positron emission (β^+) or by electron capture (EC) to give isotopes of lower atomic number. A partial list of radionuclides produced with cyclotron beams is given in attachment /Gru59/. Diagnostic or therapeutic applicability of a radiopharmaceutical depends on these physical features (type of decay and half-life). These properties and the inexpensive and easy availability of

radionuclides make them the choice radionuclides for medical uses. Although major efforts are being made in nuclear medicine for the development of therapeutic radiopharmaceuticals, it is still in its infancy /Shu04/.

1.4 Diagnostic radionuclides

Radionuclides which are useful for diagnostic applications are characterized by a number of properties. In terms of decay modes, electron capture and isomeric transition from metastable states, γ rays are appropriate. Photons with energies in the range of 100-200 keV are most suitable. Lower energy γ rays are considerably absorbed in tissue and therefore not useful for external imaging with a gamma camera, while higher energy emission leads to higher radiation dose to patients, to less imaging resolution and to reduced signal-to-noise ratios. Another group of diagnostically used radionuclides are β^+ -emitters, such as ^{11}C and ^{18}F . In terms of decay, their positron annihilation results in two photons of 511 keV, which not only allow imaging but also quantitative evaluation of radioactivity distribution. However, high cost and in this case the short half-lives of these radionuclides limit their application (Table 2). The radionuclides in demand in regular medical diagnosis would continue to be $^{99\text{m}}\text{Tc}$, ^{131}I , ^{201}Tl , ^{111}In , ^{123}I and ^{18}F . A substantial part of the use of ^{201}Tl for cardiac studies is likely to be carried out with $^{99\text{m}}\text{Tc}$ radiopharmaceuticals due to cost advantage and ready availability /IAEA03, 04/Cho01/.

1.5 Therapeutic radionuclides

Radionuclides for use in therapy are characterized by high linear energy transfer (LET) radiation like β^- , Auger-electron or α -emission. Simultaneous γ -radiation would allow to determine the therapeutic agent's distribution in patients, but also contribute to the total body radiation dose /Mic03/. In terms of radiation range. β -emitting radionuclides would be advantageous because their radiation extends beyond the bound target cell and can therefore kill surrounding tumor cells, whereas Auger-electrons and α -emitters have such a short-ranged energy deposition requiring internalization and translocation of the radiation source to the nuclear DNA to kill the

tumor cells effectively /Lim98/. Thus, the advantage of a low whole body radiation dose is counter-balanced by the ineffectiveness of radiation not taken up into the tumor cells. The physical half-lives of therapeutic radionuclides are utterly more critical than in case of diagnostic applied radionuclides. They need to be well matched with the *in vivo* tumor uptake and clearance properties of the labeled carrier-molecule /Vol91/.

Since ^{111}In emits not only photons but also auger-electrons emitter (it has a very short penetration range (0.02-10 μm) in tissue (cell diameter $\approx 10\mu\text{m}$)), therapeutic applications with ^{111}In might be possible too /Lab03/. This means that ^{111}In can potentially be used if the complex containing the nuclide could be internalized in the target cell. This would allow the Auger electrons to interact with critical cellular function particularly the DNA while causing minimal toxicity to normal cells /Shu04/Mic03/.

Table 1-2 shows some information and physical characteristics for a few radionuclides which are used in medical purposes. .

Table 1-2: Radionuclides suitable for diagnosis or therapy

Radiation	Nuclide	Physical Half-life	E_{max} [MeV]	Range in tissue at maximal energy	E_{γ} [MeV]
γ	I-123 In-111 Tc-99m	13.2h 2.8d 6.0h	- - -	- - -	0.159(83) 0.173(88), 0.247(94) 0.140(85)
β^+	C-11 F-18 N-13 O-15	20min 110min 10min 2min	1.0 0.6 1.2 1.7	0.56 mm 0.44 mm 0.78 mm 2.10 mm	0.511 0.511 0.511 0.511
β^-	Ag-111 Cu-67 I-131 Lu-177 P-32 Re-186 Re-188 Y-90	7.5d 2.6d 8.0d 6.7d 14.3d 3.8d 17.0h 2.7d	1.05 0.57 0.81 0.50 1.71 1.07 2.11 2.27	4.8 mm 1.8 mm 2 mm 1.5 mm 8.7 mm 5 mm 11 mm 12 mm	0.342(6) 0.184(48) 0.364(81) 0.208(11) - 0.137(9) 0.155(15) -
Auger	Ga-67 I-123 I-125 In-111	3.3d 13.2h 60.0d 2.8d	0.01 0.03 0.03 0.03	10 nm 10 nm 10 nm 10 nm	0.090(24) 0.159(83) 0.027(74) 0.173(88), 0.247 (94)
α	At-211 Bi-212	7.2h 1.0h	6.8 7.8	65 μ m 70 μ m	- 0.720

1.6 Indium-radioisotopes in different research

The demand for indium is increasing rapidly in recent years for various industrial, scientific and medical purposes. Indium is a group B(III) heavy metal of the periodic table, distributed in a minute quantity, about 0.1 μ g/g of earth's crust, in nature. In modern industry, indium compounds are mainly used in decorative coating, bearing, low-melting alloys, glass-sealing alloys, brazings, semiconductor research, indium solar batteries, Indium tin oxide (ITO) transparent electrodes for liquid crystal displays, nuclear reactor control rods and in nuclear medicine /Zhe93/Ino94/. As are showed in tables above and search in many literatures, it has several medically useful radionuclides, which have made extensive contribution in both the diagnosis and therapy of disease. A variety of factors contribute to the utilization of these nuclides. The first and foremost are the useful physical characteristics of the

radionuclides. These characteristics have prompted investigators to combine the nuclides with molecules that direct the nuclides to their intended target to identify some significant clinical conditions [Mic03]. Indium isotopes namely ^{113}In , ^{110}In , ^{111}In and $^{114\text{m}}\text{In}$ are widely used in therapeutic and diagnostic nuclear medicine [Eij97/Lim98/ToI00]. The important nuclear characteristics for some Indium radioisotopes which are useful in nuclear medicine are shown in table 2-3. Of the other radionuclides of indium, ^{111}In is one of the 10 most used radio nuclides for nuclear medical applications. In TDPAC (time differential perturbed angular correlation) researches ^{111}In plays an even greater role [Fil01]. The production of high purity ^{111}In ($T_{1/2} = 2.8 \text{ d}$) cyclotron produced radioisotope, which is widely used in nuclear medicine, is the major aim of this work.

A wide variety of radiopharmaceuticals have been developed using this nuclide. The most widely used is ^{111}In WBC. In addition, a number of clinical investigations are in progress in which antibodies and peptides labeled with ^{111}In are the subject of therapeutic and diagnostic evaluations [Ron03]. It is interesting to say that, $^{114\text{m}}\text{In}$ and its daughter radionuclide ^{114}In are usually regarded as undesirable long-lived impurities in ^{111}In -labeled radiopharmaceuticals for diagnostic use. However, there is increasing interest in studying $^{114\text{m}}\text{In}$ to determine long-term stability and bio kinetics of indium-labeled pharmaceuticals as well as for radionuclide therapy Low-energy [ToI02/Wei03].

Table 1-3: Important Nuclear Characteristic for Indium Isotopes^a /Wei03/

Characteristic	¹¹¹ In	^{114m} In	^{113m} In
photon energy [keV]	171 254	192 558 724	393
% photon per disintegration	91 94	17 3.5	64
Electrons [keV]	0.6 ^b 2.4, 25.4, 22.3, 19.2	1985 ^c (¹¹⁴ In)	-----
Half-life	67.4 h	50 d 100m	
Decay	EC to ¹¹¹ Cd	IT to ¹¹⁴ In, β ⁻ to ¹¹⁴ Sn	IT to ¹¹³ In
Production method	¹¹² Cd(p,2n) ¹¹¹ In	¹¹⁴ Cd(p, n) ^{114m} Cd	¹¹³ Sn
Daughter Cyclotron			¹¹² Sn(n, g) ¹¹³ Sn
Target abundance	(24%)	(28%)	(1%)
Contaminant	^{114m} In	-----	-----
Beam energy(MeV)	12-22	6.5-12.6	-----
Target yield [MBq/μA-hr]	18.5	0.8	-----
Electron structure		[Kr]4d ¹⁰ 5s ² 5p	

^a compiled from Tolmachev et al. 2000; Kowalsky&Perry 1987b; Silvester 1978; ¹¹¹In chloride, 1995; Ledere& Shirely 1978b and Thakur 1977

^b Auger electrons

^c maximum energy

1.7 ¹¹¹In production methods

As illustrated in table 1-4 ¹¹¹In can be produced by a large number of possible nuclear reactions. These reactions are classified mainly by two methods from the natural cadmium enriched or isotopes of cadmium (irradiation with protons or deuterons) and silver (irradiation with α particles or ³He ions), or by indirect formation via the precursors ¹¹¹Sb and ¹¹¹Sn /Lev74/Mac75/Bro72/Zai90/.

Table 1-4: The thresholds and Coulomb barriers for the reactions leading to production of ^{111}In

No	Reaction	Natural abundance of target isotope (%)	Q-value (MeV)	Threshold energy (MeV)	Height of Coulomb barrier (MeV)	Effective Coulomb barrier (MeV)
1	$^{111}\text{Cd}(p, n)^{111}\text{In}$	12.75	-1.63	1.63	8.49	4.11
2	$^{112}\text{Cd}(p, 2n)^{111}\text{In}$	24.07	-11.02	11.10	8.47	4.10
3	$^{113}\text{Cd}(p, 3n)^{111}\text{In}$	12.26	-17.56	17.72	8.45	4.09
4	$^{114}\text{Cd}(p, 4n)^{111}\text{In}$	28.86	-26.60	26.80	8.43	4.09
5	$^{110}\text{Cd}(d, n)^{111}\text{In}$	12.39	3.10	0	8.15	5.09
6	$^{111}\text{Cd}(d, 2n)^{111}\text{In}$	12.75	-3.85	3.92	8.13	5.08
7	$^{109}\text{Ag}(^3\text{He}, n)^{111}\text{In}$	48.65	6.55	0	15.52	10.92
8	$^{109}\text{Ag}(^4\text{He}, 2n)^{111}\text{In}$	48.65	-14.03	14.50	15.17	10.71
9	$^{112}\text{Sn}(p, 2n)^{111}\text{Sb} \xrightarrow[75\text{ s}]{\text{EC}, \beta^+} ^{111}\text{Sn} \xrightarrow[35\text{ m}]{\text{EC}, \beta^+} ^{111}\text{In}$	0.95	-17.06	17.21	8.82	4.27
10	$^{114}\text{Sn}(p, 7n)^{111}\text{Sb} \longrightarrow ^{111}\text{Sn} \longrightarrow ^{111}\text{In}$	0.65	-35.10	35.41	8.78	4.26
11	$^{115}\text{Sn}(p, 5n)^{111}\text{Sb} \longrightarrow ^{111}\text{Sn} \longrightarrow ^{111}\text{In}$	0.34	-42.65	43.02	8.76	4.25
12	$^{116}\text{Sn}(p, 6n)^{111}\text{Sb} \longrightarrow ^{111}\text{Sn} \longrightarrow ^{111}\text{In}$	14.24	-52.21	52.66	8.74	4.24
13	$^{117}\text{Sn}(p, 7n)^{111}\text{Sb} \longrightarrow ^{111}\text{Sn} \longrightarrow ^{111}\text{In}$	7.57	-59.15	59.65	8.72	4.23
14	$^{118}\text{Sn}(p, 8n)^{111}\text{Sb} \longrightarrow ^{111}\text{Sn} \longrightarrow ^{111}\text{In}$	24.01	-68.47	69.05	8.70	4.22
15	$^{110}\text{Cd}(^3\text{He}, 2n)^{111}\text{Sn} \longrightarrow ^{111}\text{In}$	12.39	-5.62	5.77	15.82	11.13

The list of reactions given in this table is not exhaustive. Atomic mass taken from Moller and Nix /Mol96/ were used in the Q-value calculations. For determining the laboratory energy of projectile necessary to provide the nuclear reaction, the energy thresholds have been calculated. Another factor of equal importance is the coulomb barrier. The heights of the coulomb barriers and the effective barrier (accounting for the tunneling effect (Münzel, 1974) are also listed in table 1-4. A consideration of the energy thresholds and barriers shows that ^{111}In can be produced using compact cyclotrons, but some of the reactions demand higher energy machines /Zai90/. It is possible to have a comparative study of all these routes on ^{111}In to determine the one best suited for compact, multiparticle, moderate energy cyclotrons. To meet the demands for ^{111}In for clinical investigations most economically, it is desirable to

minimize initial cost of targets and to avoid tedious chemical recovery of isotopically enriched target material after bombardment. Therefore the major routes of production of ^{111}In are through irradiation of cadmium targets with protons or deuterons and by bombardment of silver target with alpha particle in cyclotron table 1-5. Though in the latter case the yield of ^{111}In in nuclear reactions is much lower, the undesirable $^{114\text{m}}\text{In}$ impurity is completely excluded. Both enriched and natural target materials can be used for this purpose. In the case of natural target, only commercially available natural silver and cadmium foils with a purity of at least 99.95% are employed /Röc97/Mac75/.

Table 1-5: The four suited nuclear reactions for the production of ^{111}In

Desired reaction	Target Thickness (mm)	Incident beam energy (MeV)	Yield ($\mu\text{Ci}/\mu\text{A hr}$ at EOB)	Contaminants at 48 hr (% of ^{111}In activity)	
$^{112}\text{Cd}(p, 2n)^{111}\text{In}$	0.51	22	1035	$^{114\text{m}}\text{In}$	0.5
				$^{110\text{m}}\text{In}$	0.3
				^{109}In	0.4
$^{110}\text{Cd}(d, n)^{111}\text{In}$	0.25	12	117	$^{114\text{m}}\text{In}$	5.7
				$^{110\text{m}}\text{In}$	0.2
				^{109}In	0.02
$^{109}\text{Ag}(^3\text{He}^{2+}, n)^{111}\text{In}$	0.25	32	2	$^{110\text{m}}\text{In}$	21
				^{109}In	126
$^{109}\text{Ag}(^4\text{He}^{2+}, 2n)^{111}\text{In}$	0.064	24	55	$^{110\text{m}}\text{In}$	0.7
				^{109}In	0.6

Table 1-4 and 1-5 summarizes the results of ^{111}In productions. The reaction $^{109}\text{Ag}(\alpha, 2n)^{111}\text{In}$ shows quite good yield and has the distinct advantage that no long-lived (49,5 d) $^{114\text{m}}\text{In}$ is produced, whereas variable amount of this undesirable contamination are always present in ^{111}In derived from p-induced reaction on Cd targets. On the other hand the $^{112}\text{Cd}(p, 2n)^{111}\text{In}$ reaction has excellent yields (20 times better than the ^{109}Ag reaction) so this reaction is very attractive and might be preferred. Table 5 shows that besides ^{111}In from the $^{112}\text{Cd}(p, 2n)^{111}\text{In}$ reaction also $^{114\text{m}}\text{In}$ ($T_{1/2}$ 50.0 d) is produced. This long-lived radionuclide is undesirable due to the increased radiation dose to the patient. It is known /Mac75/Bro72/ that $^{114\text{m}}\text{In}$ production results from $^{114}\text{Cd}(p, n)^{114\text{m}}\text{In}$ reaction (figure 2-1). The use of high energy protons >22 MeV, significantly reduces the amount of $^{114\text{m}}\text{In}$ produced. Nevertheless especially for laboratories with cyclotrons not capable of producing high energy protons, reactions with targets highly enriched in ^{112}Cd are preferred.

Table 6 shows the energy and the cross section for $^{112}\text{Cd} (p, 2n)^{111}\text{In}$ /Tak04/IAEA03/.

Table 1-6: Recommended cross sections for $^{112}\text{Cd} (p,2n)^{111}\text{In}$ reaction

Energy	Cross section						
(MeV)	(mb)	(MeV)	(mb)	(MeV)	(mb)	(MeV)	(mb)
9.5	6.6	16.5	828.6	23.5	861.2	30.5	212.4
10.0	13.8	17.0	879.7	24.0	813.9	31.0	187.3
10.5	24.7	17.5	918.6	24.5	760.9	31.5	167.0
11.0	42.4	18.0	946.8	25.0	704.5	32.0	152.0
11.5	69.8	18.5	966.1	25.5	646.7	32.5	141.4
12.0	110.0	19.0	978.2	26.0	589.3	33.0	134.3
12.5	165.8	19.5	984.4	26.5	533.6	33.5	129.5
13.0	237.2	20.0	985.7	27.0	480.7	34.0	126.0
13.5	321.5	20.5	983.1	27.5	431.6	34.5	122.8
14.0	412.3	21.0	977.1	28.0	386.5	35.0	118.9
14.5	506.3	21.5	967.6	28.5	345.4	35.5	114.3
15.0	599.8	22.0	953.0	29.0	307.7	36.0	109.2
15.5	687.2	22.5	931.3	29.5	273.0	36.5	103.6
16.0	764.2	23.0	900.9	30.0	241.2	37.0	97.8

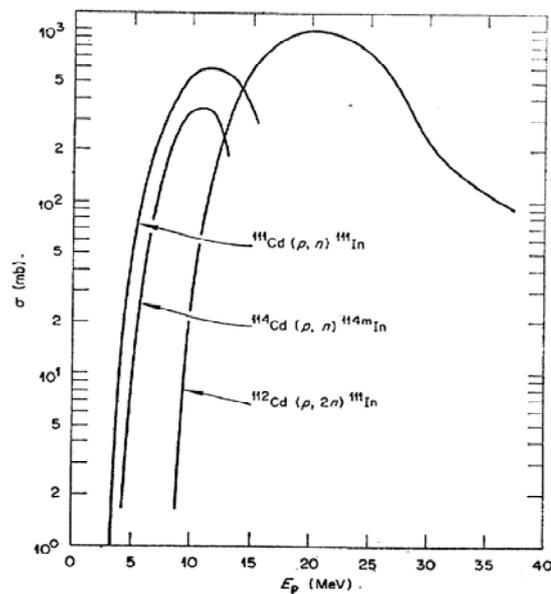


Figure1-1: Excitation function (reaction cross sections) for different proton energies (E_p)/Mac75/

The figure 1-1 has shown the bombardment of natural cadmium with protons at the maximum available energy (22 MeV) is by far the most rewarding method for ^{111}In production. It is necessary however to strike a compromise between the increase in yield of ^{111}In afforded by making the target thicker, and the concomitant rise in unwanted $^{114\text{m}}\text{In}$ /Mac74/Bin04/.

As we can see in table 1-6, when preparation of ^{111}In is carried out by bombarding the Cd target with proton (deuteron) the ^{111}In activity at the end of bombardment (EOB) contains undesirable contaminations of other indium radionuclides ^{109}In ($t_{1/2}=4.3\text{h}$), $^{110\text{m}}\text{In}$ ($t_{1/2}=4.9\text{h}$) and $^{114\text{m}}\text{In}$ ($t_{1/2}=4.9\text{d}$). The first two radioisotopes of indium have relatively short half-life and a suitable waiting period is required after EOB to diminish drastically their activities. The chemical separation must not be performed before at least 99% of these two radioisotopes have decayed. The later nuclide $^{114\text{m}}\text{In}$ has a significant meaning due to the radiation dose to patients receiving ^{111}In radiopharmaceutical containing as contamination this long-lived radionuclide. The $^{114\text{m}}\text{In}$ contamination should be reduced to the lowest level (accepted by nuclear medicine) /Zai90/.

Undesirable $^{114\text{m}}\text{In}$ is always present in the final indium fraction derived from a cadmium target irradiated by protons. Its level changes from 0.003% (Beavie et al., 1978) to 3% (Mc Donald et al., 1975).

Mac Dowell et al are reported that, in a stacked foil experiment, the front 0.254 mm Cd foil produced only 0.56mCi/ μAhr of protons, calculated at the end of bombardment (EOB). Foil totaling 0.51mm in thickness yielded 1.03 mCi/ μAh , with $^{114\text{m}}\text{In}$ activity amounting to 0.56% of the ^{111}In activity at EOB. Increasing the total thickness to 0.76mm increased the yield of ^{111}In substantially (1.31mCi/ μAhr), but unfortunately also raised the proportion of $^{114\text{m}}\text{In}$ to 0.92%. This level of $^{114\text{m}}\text{In}$ would cause an unwanted increase in radiation dose to patients receiving ^{111}In solutions containing this contaminating radionuclide, principally because of its 50-days physical half-life. Therefore the routine Cd-targets shall never exceed 0.51mm in thickness then the $^{114\text{m}}\text{In}$ contamination will be less than 0.35% at EOB. The same situation will be observed with deuterons. The highest yield of ^{111}In will obtained with

Cd-targets thick enough for total absorption, but the ^{114m}In contamination will be intolerable 9.8 %.

A lengthy "cooling-off" time is required to permit decay of the products of proton reactions with other Cd isotopes, notably 4.3 hr ^{109}In and 4.9 hr ^{110m}In . The latter is undesirable because its high energy gamma-rays would seriously degrade the spatial resolution of gamma-ray scintillation cameras and scanners attempting to image the distribution of ^{111}In in patients. The ^{109}In is troublesome for an additional reason. It decays to 453 days ^{109}Cd , whose administration to patients should be avoided. Therefore the chemical isolation of ^{111}In from the bombarded, raw Cadmium target must *not* be performed before at least 99% of this ^{109}In has decayed, otherwise it will accompany ^{111}In through the chemical separation steps into the final solution where it will then decay to the undesirable ^{109}Cd /Röc97/San97/. Careful analysis of the gamma-ray spectrum of the ^{111}In production immediately after its chemical isolation shows also the presence of a small amount of 4.5 hr ^{115m}In . This is attributed to the "in-growth" of ^{115m}In from its parent ^{115}Cd (53.5 hr half-life) during cooling of the target before chemical extraction. The ^{115}Cd , in turn, probably arises from the (p, xn) reaction on stable ^{116}Cd , whose natural abundance is 28.8%. When the chemical isolation procedure is performed 48 hr after EOB, the amount of ^{115m}In activity measured immediately therefore is only 0.45% of ^{111}In activity and diminishes rapidly. Therefore this ^{115m}In is not a significant contaminant for medical purposes.

Mac Dowell et al finds that it is practical to wait 48 hr after EOB before chemically isolating the radio indium, by which time the ^{109}In and ^{110m}In activities have both dropped to less than 0.4% of the ^{111}In . Of course, this is achieved at the cost of losing also by decay, 39% of ^{111}In available at EOB. Accepting this loss, they find that bombardment of natural Cd metal foil with 22 MeV protons for 2.0 hr at a current of 30 μA provides, 48 hr later, 30-35 mCi of ^{111}In suitable for medical use. With cyclotrons equipped for bombardment of targets internally, where currents of 100-200 μA are attainable, the yields of ^{111}In can be expected to be three to six fold greater for the same bombardment time. /Mac74/Fil01/Bro72/Mil04/.

^{111}In decays by electron capture to stable ^{111}Cd , with the two emission of gamma rays of 0.171 and 0.245 MeV, which are accompanied by total internal conversions

of about 10% and 6% respectively /Mac74/. A partial decay scheme for ^{111}In and $^{111\text{m}}\text{Cd}$ is shown in Fig.2 /Shp02/Ame04/.

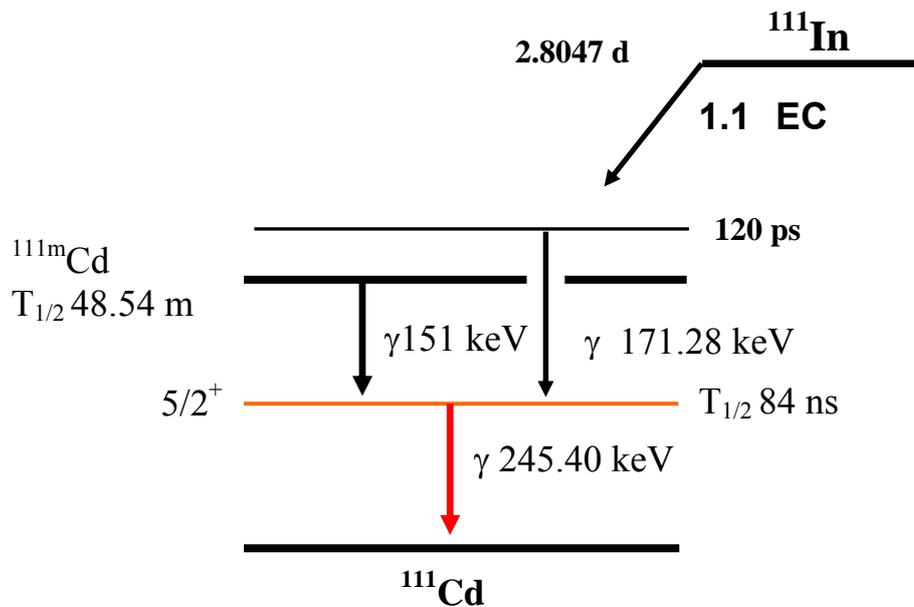


Fig 1-2: Partial decay scheme for ^{111}In and $^{111\text{m}}\text{Cd}$. The half-life of each level is labeled. The 171-245 keV gamma cascade follows the electron capture decay of ^{111}In ; the 48.5 minute $^{111\text{m}}\text{Cd}$ state decays the 151-245 keV gamma cascade. Both cascades share the same 245keV $5/2^+$ ^{111}Cd intermediate nuclear state. /Shp02/Fil01/.

1.8 ^{111}In characteristics and medical applications

As we discussed above, ^{111}In by virtue of its suitable characteristics (2.8 days, EC, γ -emission), absence of β -emission and low $\tilde{\gamma}$ emission of 171 keV (89%) and 254 keV (94%) is well suited for diagnostic nuclear medicine. Medical investigators have shown that ^{111}In is an important radionuclide for locating and imaging certain tumors, visualization of lymphatic system and thousands of labeling /And99/ Kel04/. The 67 hr physical half-life respectively is well suited for several in vivo applications (e.g. the study of slow biological processes, for which observation periods of 1-3 days after administration are necessary) /Pai01/Dah72/Mac74/Gru58/Tha71/. Among many

diagnostic nuclear medicine procedures the most important involve the use of ^{111}In -labelled blood cells, ^{111}In -labelled monoclonal antibodies, ^{111}In DTPA and ^{111}In leukocytes, ^{111}In labeled human gut-derived T cells, ^{111}In chloride /Fil01/Lev73/Mic03/Lim98/Tol00/And99/.

This half-life allow in vitro studies to be carried out for several days without having to administer excessively large quantities of radioactivity, specially for labeling proteins and peptides and also used in Lymphoscintigraphy, infection imaging, cisternography, and has high potential for use in radioimmunology scintigraphy /Das96/. A number of efficient tumor seeking pharmaceuticals have been developed and labeled with ^{111}In (e.g., octreotide, bleomycin and monoclonal antibodies. An individual dosimetric evaluation before treatment can be performed using positron emission tomography (PET) and single photon emission computed tomography (SPECT) by labeling the carrier molecule by positron emitting ^{110}In as well as commercially available ^{111}In /Tol00/. Comparative dual-labeling studies have demonstrated that indium is retained in tumor tissue longer than the radioisotopes of iodine and rhenium, which commonly are used for radionuclide therapy /Van03/Sea04/Shi94/Bro03/Ray01/. And many other different procedures and methods for medical applications which are commonly widely used, e.g. [^{111}In]-diethylenetriamine pentaacetic acid (DTPA)-D-phe-octreotide (OctreoScan111[®]), which is routinely used for localization of neuroendocrine tumors expressing somatostatin receptors /Tol00/ and has also been applied for therapy in patients with such tumor types. This radiopharmaceutical is optimized for labeling with radioindium and its pharmacokinetics have also been studied /Eis66/Ray01/.

1.9 ^{111}In separation and purification methods

It is well known that the radionuclide, when used for medical purposes, has to be both chemically and radio chemically pure. Stringent conditions are imposed for the purity of the substance. Thus a method of preparing, ^{111}In radioisotope in high nuclidic and chemical purity is needed /Das96/.

Methods for radiochemical separation of ^{111}In include, co-precipitation with $\text{Fe}(\text{OH})_3$ /Nei70/, ion exchange /Das96/Mal97/, extraction chromatography /Lev73/

Sha81/Hor97/ and thermo-chromatography /Nov84/Sch88/, use of cation exchange Resin /Bro72/Mal97/Nel66/San97/, co-precipitation with $\text{La}(\text{OH})_3$ /Fil01/, liquid-liquid extraction using Cyanex923 /Bin04/, liquid-liquid distribution of ion associates of tetrabromoindate (III) with quaternary ammonium counter ions /Koi77/, using organophosphorus compounds as extractants /Nis98/Raj94/, extraction chromatography using liquid anion exchanger /Hor95/ and solid phase extraction /Hom95/Hor90/Hor91/. Each of the methods has advantages and disadvantages. Until now two of these methods are widely used for radiochemical separation of, liquid-liquid extraction (LLE) /Ino94/Zeh93/Pai01/Hor93-95/ and ion-exchange chromatography (IEC) /Hor90-97/San97/Bin04/Nov84/Nis98/Raj94/Ham95/.

1.10 Liquid–Liquid Extraction

LLE tends to be highly specific since extraction conditions and supporting complexing agents can readily be introduced to the separation and might easily be optimized. On the other hand extraction procedures are time-consuming, generate substantial volumes of organic waste (rather large amounts of radioactively contaminated organic waste are produced) and have limited effectiveness in removing certain common matrix components (notably iron). These drawbacks make Liquid-liquid extraction unattractive for routine use on large numbers of samples /Hor90/. Furthermore, LLE methods are not easy to handle.

In comparison to that IEC does show a lack of selectivity, though selectivities might be enhanced by optimizing the eluent and by adding complexing agents. Since mixing of liquids is not needed. It will be do just by passing aqueous solutions through an ion-exchange column. IEC separations are generally very easy to handle. Because of the rather low selectivities and slow kinetics of the IEC-materials columns with large bed volumes and slow flow rates have to be used in order to achieve good separation factors, making the separations very time consuming.

1.10.1 Solid Phase Extraction (SPE)

The more modern technique of solid-phase extraction (SPE) combines the high-selectivity of LLE-methods with the easy handling of IEC-Methods.

The solid-phase consists of a supporting inert polymer, organic or inorganic, on which a highly selective extracting agent, often derived from experiences with LLE separations, dissolved in an organic diluent, is adsorbed /Pai01/ Zai90/Iza96/.

Due to their high selectivities and fast kinetics SPE materials allow the use of small columns and high flow rates, thus saving operating time.

SPE-Methods are widely used in analytical applications, mainly in the separation of α - and β -emitting nuclides /Gur58/Moi96/Das96/ and have proven to be powerful tools in separation chemistry.

The high selectivities obtainable make them the preferable material for the preparation of high-purity solutions.

For Indium/Cadmium separations four different materials are likely to be useful. TEVA, TRU, Ln and Ac resins.

TEVA Resin® consists of Aliquat-336® sorbed on a polymeric support and is based on the principles of ion-pair extraction /Eic99, Hor00/.

The active component of TEVA Resin® is aliphatic quaternary amine. As such it has properties similar to those of typical strong base anion exchange resins. The uptake of these ions is generally higher and often at lower acid concentrations.

In earlier studies /Zhe93/Koi77/Nis98/ it was shown that Aliquat-336® is very well suited for the preconcentration of Indium and the removal of Iron and Copper impurities, originating mainly from the backing of irradiated targets.

Furthermore, it has been suggested /Zhe93/Koi77/Nis98/Raj94/ that organophosphorus chelating agents might be useful for the selective extraction of Indium. TRU Resin®, Ac Resin® and DIPEX Resin® were chosen, since all of them are comprised of such chelators. In addition to that it is known that TRU Resin®, DIPEX Resin® and Ln Resin® preferably extract trivalent cations even in presence of large excess of divalent cations, which will certainly help achieving quantitative Indium/Cadmium separation.

Actinide-resin is based on the DIPEX extractant. The resin exhibits an extraordinarily high affinity for the actinide elements /Hor97/.

Ln Resin, is also grew out of the transformation of a selective organic extractant into an extraction chromatographic resin. The extractant used in Ln Resin is di(2-ethylhexyl) orthophosphoric acid (HDEHP). And the TRU Resin is based on extractant system, octylphenyl-N,N-di-isobutyl carbamoylphosphine oxide (abbreviated CMPO). dissolved in tri-n-butyl phosphate (TBP) /Hor93/.

1.10.2 Aim of this work

The preparation of high-purity ^{111}In solutions from irradiated targets, especially ^{112}Cd targets for medical purposes is the major aim of this project. Furthermore a fast and convenient way for further in-hospital purification of ^{111}In solution shortly before its use shall be developed. In addition to that highly enriched ^{112}Cd is expensive, so the recovery of enriched ^{112}Cd from dissolved targets have been achieved.

All of the extraction materials do show limited capacities of very few mg per mL of resin, according to that finding condition that allow selective extraction of Indium is crucial since it has to be extracted from large excess of Cadmium. As it can be seen in the later of this work, (SPE) is a fast and convenient way for further in-hospital purification of ^{111}In solutions shortly before its use for medical purposes. All activities were determined by liquid scintillation spectrometry (LSC) and /or gamma spectrometry, some trace elements contamination of sample solutions such as Fe, Al and Cu were determined by Inductively Coupled Plasma-Optical Emission Spectroscopy (ICP-OES) method.

Further more a very important experiment has been done with real target at Jülich research center (JFZ) in order to produce High purity ^{111}In from bombardment of high pure natural cadmium targets at CV-28 Cyclotron.

2 Counting Techniques

2.1 Radiometry

Radiometric instruments utilize the phenomenon associated with the decay of radioactive substances, and the emissions of sub-atomic particles that is associated with this process, to the source of the emission.

The luminescence produced when radiation strikes a phosphor represents one of the oldest methods of detecting radioactivity and X-rays, and one of the newest as well. Liquid scintillation is one of the techniques relying on this phenomenon /Som03/.

Among the various radiation detecting methods, the liquid scintillation counting system is primarily used for detection of alpha and beta rays.

Liquid scintillators can and have been used to measure almost every kind of radioactive decay: negatron, positron, electron capture, gamma, alpha, fission, proton, neutron, neutrino, cosmic rays, etc. The relative scintillation yield is defined as the photon yield (or pulse height response) per unit energy deposited in the scintillators solution. This yield depends not only on the energy of the particle but on the type of particle causing the production of excited molecules /Hor64/Tha-ABA008/. In each case the scintillation yield has been normalized relative to an electron-- table 2-1.

Table 2-1: Relative scintillation yield per million electron volts for different types of particles exciting a liquid scintillator

Particle	Relative scintillation yield
Electron	1
Proton	0.5
Alpha	0.12-0.08
Fission	0.013

2.1.1 Counting beta and electron emitters

Both types of particles, negatively and positively charged electrons, interact with liquid scintillators counter in the same manner. They produced a continuum of pulse heights corresponding to the continuum of beta energies, zero to maximum. The only difference is that when the positron is completely stopped, i.e., at zero kinetic energy, two gamma rays of 0.51-MeV are produced. For most small-volume LS (20mL), these gamma rays are not detected /Hor74/.

Internal conversion and electron capture are also electron producers. These electrons produced are mono energetic or groups of mono energetic electrons as opposed to the energy continuum of electrons produced by beta decay.

2.1.2 Counting electron capture

Radioactive decay by electron capture leads to the production of Auger electrons. The yield of Auger electrons is:

$$\omega_{\text{Auger}} = 1 - \omega_X \quad (2-1)$$

For a vacancy in the K shell of the nuclide, the fluorescence yield ω_X is the probability that a K X-ray will be formed.

When the K X-ray is not formed the energy is transferred to an electron, and the electron will have an energy equal

$$E_{\text{Auger}} = E_{\text{K X-ray}} - E_{\text{binding}} \quad (2-2)$$

The subsequent rearrangement will lead to the production of more Auger electrons and characteristic X-rays. In those cases where the secondary X-rays are low and thus totally absorbed in the scintillators solution, the total energy deposited in the scintillators solution will be the binding energy of the initial captured electron.

2.2 Principle of Liquid Scintillation County (LSC)

Scintillators respond directly to ionization generated by charged particles. Neutral radiations

(e.g. gamma rays and neutrons) are detected if they produce recoil electrons or recoil nuclei within the scintillators material /Kra70/.

Liquid scintillations instrument detect scintillations in a suitable liquid such as p-terphenyl in toluene, produced by low energy beta radiation from radioisotopes such as carbon-14, sulphure-35 and tritium. The sample is generally dissolved in a solution of the scintillation liquid. A vial containing the solution is then placed between two photomultiplier tubes housed in a light tight container.

The process of liquid scintillation involves the detection of beta decay within a sample via capture of beta emission in a system of organic solvent and solutes referred to as the scintillation cocktail. The basis of cocktail material is, mostly Alkyl Benzene, such as Tolol, Xylol, Triethylbenzol or Dodecylbenzol, Phenylcyclohexan, and ever more frequently the less toxic solvents Pseudocumul Diisopropylnaphthalin(DIPN), Ethylnaphthalin, Isopropylphenyl and Phenylxyloethan (PXE) /Hor74/.

This mixture (cocktail) is designed to capture the beta emission and transform it into a photon emission, which can be detected via a photomultiplier tube within a scintillation counter. The cocktail must also act as a solubilizing agent keeping a uniform suspension of the sample.

2.2.1 Scintillation counting component

The scintillation counting system consists of three primary components: The radioactive substance, the solvent, and the solute (or fluor).

Beta or other radio active particles are emitted, which cause solvent molecules to become excited Fig. 2-2.

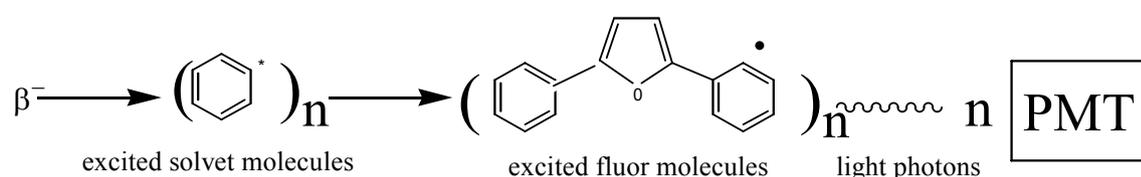


Fig 2-2: The energy of the solvent molecules is transferred to the fluor molecules, which in turn emit light /Som03/.

The solvent is the first compound in the scintillation cocktail to capture the energy of the radio active particles. The solvent molecule achieves an excited state, and the excess energy is transferred from solvent molecule to solvent molecule. The solvent

remains in the excited state for an extended period of time, decaying into the ground state without the emission of light. The solute then absorbs the excitation energy of the solvent, and quickly returns to the ground state by emitting light. If a secondary solute is used, that solute absorbs the signal of the first solute and emits a second burst of light at a longer wavelength Fig. 2-3

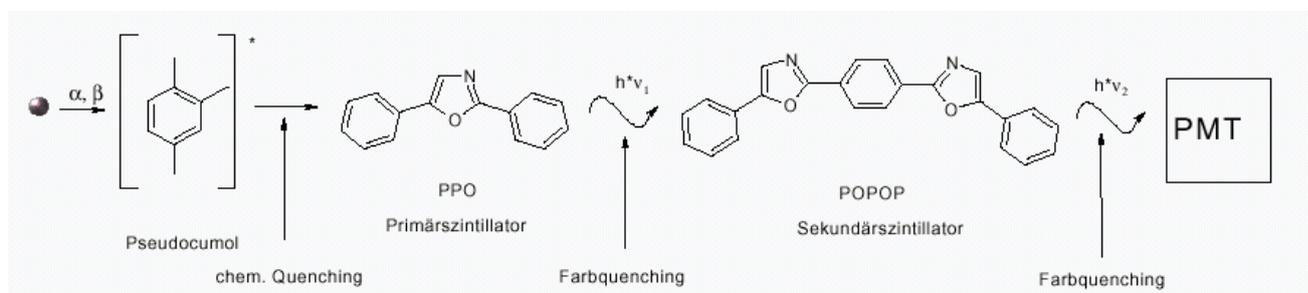


Fig 2-3: Principle of the liquid scintillation spectrometry

2.2.2 Photomultiplier

Photons of the scintillation emerge from the vial containing the scintillation solution, and are detected by a light-sensitive device known as a photomultiplier tub (PMT). The photons interact with the photocathode and eject photoelectrons. In the course of few (e.g. 12) dynode stages, the number of electrons is increased by a factor of about 10^7 ; An electrical pulse appear at the output of the PMT as a result of the photons which interacted with the photocathode. The amplitude-height-of this pulse (as a voltage) is proportional to the number of photons which interact with the photocathode; the pulse height at the output of the PMT is proportional to the energy of the beta particle in the sample /Tri84/.

2.2.3 Energy transfer in liquid scintillation solutions

The response of scintillators materials to charged particles can be described by a relation between dL/dx , The fluorescent energy emitted per unit path length, and dE/dx , the specific energy loss for the charged particle (LET linear energy transfer) /Kno99/a. Particles with different LET's deposit their energy at their way in the sample very differently. In liquid scintillation counting the excitation energy is in the

form of kinetic energy of an ionizing particle produced by a nuclear emission or as a secondary interaction of the materials in the scintillators solution with a non ionizing nuclear emission. Essentially all of the primary excitations results in the formation of excited solvent molecules. The energy then migrates from one solvent molecule to another until the energy is trapped by a solute molecule. If there is a secondary solute, the energy is subsequently transferred from the primary solute to the secondary solute where it is trapped. Finally the energy is released in the form of a photon, which characteristic of the fluorescent species /Hor74/. The scintillation efficiency fraction of ionization energy converted to fluorescent light energy, differs for each type of scintillators and also depends on the type of charged particle producing the ionization. Electrons generate more light than do heavy particles (e.g. protons and ⁴He particles) of equal energy when stopped in organic scintillators

Briks has derived a formula which has been extremely successful in explaining many of the features of the experimental data for organic scintillators. His treatment assume that high ionization density along the particle track is responsible for the quenching effect which is observed for protons and other heavy ionizing particles. The quenching of the primary ionization energy is believed to occur within a time that is short compared with the fluorescence decay times (<1 nsec) /Cra70/.

In the absence of quenching, the light yield is proportional to energy loss /Kno99/ (Ideal case of fluorescence):

$$\frac{dL}{dx} = S \frac{dE}{dx} \quad (2-3)$$

Where S is the normal scintillation efficiency. To account for the probability of quenching, Briks then writes

$$\frac{dL}{dx} = \frac{S \frac{dE}{dx}}{1 + kB \frac{dE}{dx}} \quad (2-4)$$

Brik's formula

Equation (2.4) is commonly referred to as *Briks' formula*, where kB is treated as an adjustable parameter to fit experimental data for a specific scintillators. In many case the value of S providing the absolute normalization.

For particles with very small specific energy loss (dE/dx), like approximately a fast β⁻, equation 2-4 changes again into equation 2-3, since very small Quench is taking place (very small KB).

$$\frac{dL}{dx}|_e = S \frac{dE}{dx} \quad (2-3)_a$$

This is the ideal case, since under these conditions fluorescence emitted per deposited energy, is a constant

$$\frac{dL}{dx} = S|_e \quad (2-5)$$

Fluorescence per delivered energy, (fast β^- particle)

This is the regime in which the light out put

$$L \equiv \int_0^E \frac{dL}{dE} dE = SE \quad (2-6)$$

is linearly related to the initial electron energy E.

On the other hand, for an alpha particle, dE/dx is very large so that saturation occurs along the track and Briks' formula becomes

$$\frac{dL}{dx}|_\alpha = \frac{S}{kB} \quad (2-7)$$

In order to match experimental data more closely, other formulas for dL/dx have been proposed by a number of authors. These are semi empirical formulas that introduce one or more additional fitting parameter /Kno99/a.

Many investigations have been done and received data attempted to describe an extended Briks' formula, and whereby with C a further empirical parameter was introduced /Cra70,Smi68/.

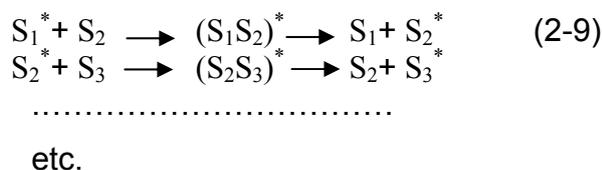
$$\frac{dL}{dx} = S \frac{dE}{dx} \left[1 + kB \frac{dE}{dx} + C \left(\frac{dE}{dx} \right)^2 \right]^{-1} \quad (2-8)$$

Extended Briks' formula

Where C is again treated as an empirically fitted parameter. This expression approaches the simple Briks' formula Eq (2-4) for small values of dE/dx .

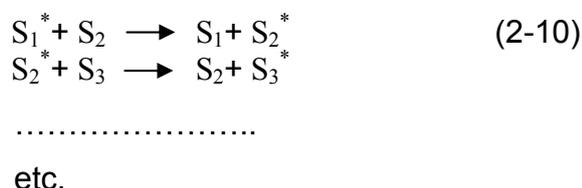
2.2.4 Energy transfer between solvent molecules

For the energy transfer between two solvent molecules two mechanisms are discussed. Briks /Bir64b, Bir71/ suggests a mechanism which is based on the formation of solvent excimers. This solvent excimer formation and breaking up occurs many times, allowing the energy to migrate a long distance in the time, which is very short compared to the fluorescence emission time:



Each of these reactions is equilibrium. Thus it is possible to have excimer formation and breaking apart without energy transfer.

A second theory involves energy migration from one solvent molecule to its adjacent neighbours/Hor74/.



Both of these mechanisms explain the observed evidence of energy transfer between solvent molecules. The energy transfers are monoenergetic. The excited state responsible for the energy exchange is most probably the first excited singlet state (S_1).

2.2.5 Solvent molecule-scintillator energy transfer

The energy transfer between the solvent molecules and the scintillators molecules are non radioactive, the energy transfer occurs by a resonance transfer process /Hor74/. The distance over which the transfer will occur is related to the extinction coefficient of the acceptor molecules (Scintillator molecule in the initial state) /Hap03/

over the region of overlap of the two spectra (emission of the donor and absorption of the acceptor).

2.2.6 Fluorescence

In Fig. 2-4 /Hor74/ is shown a modified Jablonski diagram (31) of various processes that can occur when a molecule is excited. The general term *luminescence* is used to describe the emission of light from an excited species; *fluorescence* describes emission from the singlet excited states, usually the S_1 excited state; and phosphorescence is the emission from the triplet excited state.

Fluorescence decay times are very short, of the order of 10^{-5} - 10^{-9} sec. Most organic scintillator solute have decay time of a few nanoseconds. In liquid media the triplet state emission is not observed because of the long life of the triplet state, the triplet energy is usually lost through quenching.

Fluorescence usually occurs between the first excited state (S_1) and the ground state of the given molecule. The energies of the photons (emission) cover a rather wide band, corresponding to the energy difference between the zero vibrational level of the S_1 state and the many vibrational levels of the ground state.

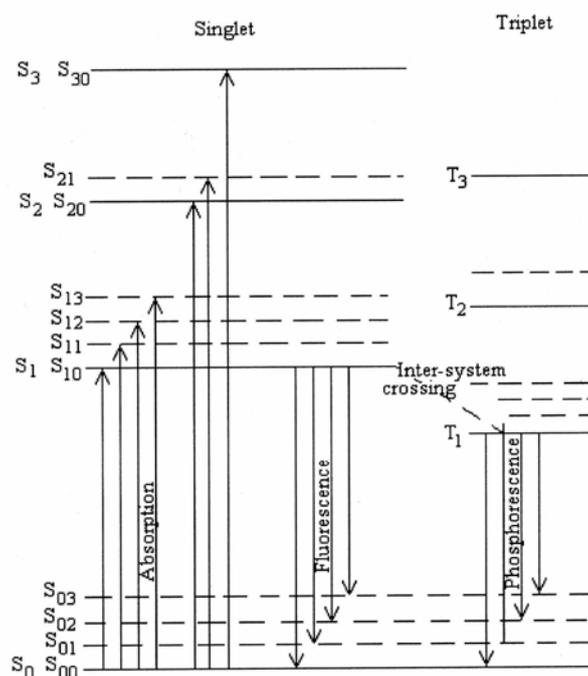


Fig 2-4: Modified Jablonski diagram showing the various processes that can occur upon excitation of an organic molecule

The types of fluorescence transitions are schematically shown in Fig. 2-5. Most organic scintillators solute have fluorescence spectra that have several peaks of different intensity. The transition between S_{10} and low vibrational levels of the ground state is the most probable.

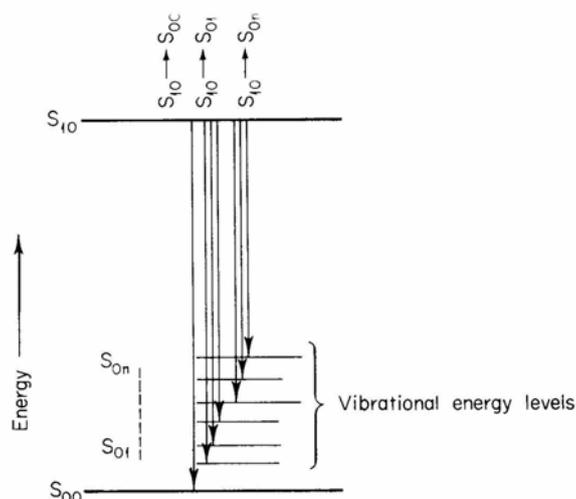


Fig 2-5: Fluorescence transitions between first excited singlet state (s_{10}) and vibrational of the ground state (S_{0n})

2.3 Background

There are many sources which causes background (cpm) in liquid scintillation counting. The main division of these sources is into those produced in the liquid scintillators solution and those which result from events that have no connection with the liquid scintillators solution (table 2-2).

Table 2-2: Summary of the common background sources

Source	Contribution
Liquid scintillator materials	<ul style="list-style-type: none"> • Natural radioactivity in the materials which constitute the liquid scintillators • Chemiluminescence, bioluminescence and phosphorescence of certain solvents enhanced by the presence of the solutes
Sample	<ul style="list-style-type: none"> • Natural radioactivity in the sample which may be the same or different from the nuclide to be assayed • Contamination with the same or other radioactive material Chemiluminescence and phosphorescence produced by the sample or impurities in the sample
Vial	<ul style="list-style-type: none"> • Natural radioactivity in the vial walls or cap • Cosmic-Ray-induced background-Cerenkov and secondary electrons and gamma rays • Static charge build-up during movement in the sample changer
PMT	<ul style="list-style-type: none"> • Natural radio activity in materials which make the PMT • Cosmic rays which produce Cerenkov radiation, secondary electrons, and gamma rays • Thermionic and secondary electron emission from photocathode and dynoded in coincidence systems. This is mostly eliminated, because of its randomness • Cross talk from electric discharges and/or Cerenkov radiation after pulses
Other radioactive sources	<ul style="list-style-type: none"> • Radioactive sources (usually gamma rays) in the area of the liquid scintillation counter • The movement of these sources can be very detrimental, because it will lead to changes in the background level

2.3.1 Luminescence effect

The Luminescence effects (especially chemoluminescence and bioluminescence) produce the most important count rate as background in scintillation counting.

Chemoluminescence and bioluminescence can be viewed as a process by which certain excited electronic states are produced by the energy of a chemical reaction. Most chemical reaction converts the excess energy into kinetic energy (thermal dissipation). The luminescence-producing reactions convert the excess energy (or a fraction of it) into photons.

Chemoluminescence (CL) is the emission of photons as the result of a chemical reaction, which may involve impurities present in the scintillation solution, reagents used to solubilizing the sample, or the sample itself, and will continue as long as the chemical reactants are present. Even the highest purity of all chemicals used will not completely eliminate the possibility of CL counting. The ideal sample counting system would be one which does not have CL. The presence of CL in liquid scintillation counting is undesirable. Many techniques are offered in the literature as methods for eliminating or reducing CL /Hor74/.

2.3.1.1 Chemoluminescence

The chemical reactions with oxygen or hydrogen peroxide make the Chemoluminescence, and chemical reaction with bio molecules react as bioluminescence.

Luminescence is observed, if sufficient energy (to delivers as photon energy) is produced, with the respective reaction. The chemo and/or bioluminescence depends on the number of reacting particles and on the reaction rate /Hap03/. Chemoluminescence decrease by lowering of the sample temperature.

2.3.1.2 Photoluminescence

The term photoluminescence is used here to describe the production of photon-producing species by light, i.e., sunlight, room light, etc. Often the photoluminescence species are very long-lived, especially those produced in the vial

walls and caps, since they are not subject to the normal deactivation processes that occur in the liquid phase via collision. This long-lived photoluminescence is usually referred to as phosphorescence, although the strictest use of the term phosphorescence applies to the spontaneous emission from triplet excited state /Hor74/.

The phosphorescence fades away mostly within a few minutes, therefore keeping the samples in cold and dark place before the measurement is sufficient in order to reduce the photoluminescence.

2.4 Quench effect

Any factor, which reduces the efficiency of the energy transfer or causes the absorption of photons results in quenching of the samples. It can be says also a common problem is that the introduction of the sample tends to reduce the scintillation light output compare with the pure scintillators. This phenomenon, commonly called *quenching*, Often limits the amount of sample material that can effectively be incorporated within the scintillators solution /Kno99/. Quenching is a phenomenon which results in a reduction of the scintillation count rate. Because of the quenching, the energy spectrum detected from the radionuclide appears to shift toward a lower energy. There are three major types of quenching, all of which several to disrupt the normal chain of events in scintillation counting: photon quenching, which occurs at the level of beta emission from the radionuclides; chemical impurity quenching, which takes place either during the energy transference between solvent and solute or the fluorescent emission of the solute; and colour quenching, which transpires between the fluorescence emission and its reception by PMT /Kno99/

2.4.1 Electron capture (photon quenching)

An emitted β - particle is caught by a strongly electronegative molecule such as CCl_4 , before its kinetic energy deliver (complete) to the solvent molecules. This kind of the Quenches has direct influence on the counting rate and spectrum.

2.4.2 Color quenching

By coloured substances, as Fe^{+3} salts or organic colouring materials, a part of the emitted photons in the scintillator solution is absorbed. Thus the number of the detected photons per emitted particle is reduced, this leads to a shift of the spectrum to lower energies.

2.4.3 Concentration quenching

This kind of quenching based on the self-absorption of the scintillator molecules. The more highly concentration of the scintillators and the smaller their Stokes' Shift, causes largely quench effect.

2.4.4 Chemical quenching

By foreign matter the transfer of energy between solvent molecules becomes disturbed. Chemical quenching results from the absorption of beta energy (before being converted to photons) by organic molecules that have not been completely oxidised or combusted. In a chemically quenched sample, all energy radiations appear to be equally affected, shifting the spectrum to lower energies. The count rate is reduced as the quenching increases. The sample spectrum indicates that the lowest quenched sample spectrum can be regarded as being the true observed spectrum for the sample. Where the highest quenched sample spectrum is shown represents the situation where there has been chemical quenching that has resulted

in a shift in the spectra to lower energy and a reduction in the efficiency, as indicated by a reduced area under the spectral curve /wil01/.

2.4.5 Phase quenching

Phase quenching results from occurrence of several phases in the scintillator solution. As already explained these effects lead to a reduction of the total counting rate and to a shift of the spectrum to lower energy. An example is shown at Fig. 2-6. A ^{90}Sr standard solution, in the equilibrium with its daughter ^{90}Y , was shifted with rising quantities of a quenching agent, CCl_4 .

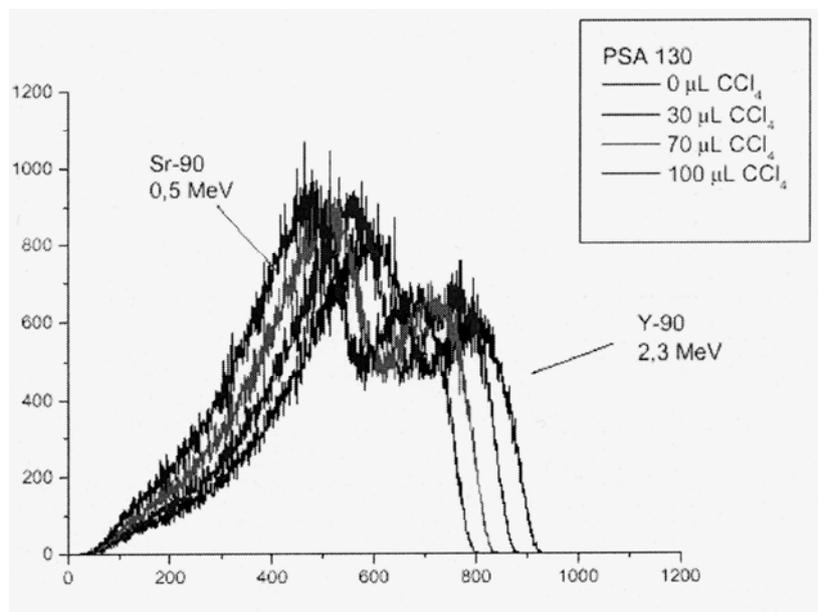


Fig 2-6: Quenching from CCl_4 in the beta spectrum from $^{90}\text{Sr}/^{90}\text{Y}$

2.5 Quench correction methods

The different amount of quench will be reflected in the counting efficiency. More quench will cause a lower counting efficiency and less quench a higher counting efficiency. The absolute change in counting efficiency will be greater as the energy range of the particle to be counted decreases.

In order to measure accurately the amount of radioactive material in liquid scintillator solutions, it is necessary to know the real counting efficiency of that nuclide.
($\text{Dpm} = \text{cpm}/\text{Eff}$)

The counting efficiency is usually determined by some method which relates to measurements made with similar samples with known amount of the same radioactive nuclide that is being counted /Hor74/.

2.5.1 Internal standard method

The internal standards method is perhaps the most accurate method of quench correction (it is probably the oldest method), and not too much usable. It involves the addition of known amount of the nuclide in high specific activity (standard) to the same sample that is being measured. Counting efficiency can be calculated from equation 2-11.

$$Eff = \frac{cpm(standard + sample) - cpm(sample)}{dpm(standard)} \quad (2-11)$$

The cpm of the standard is usually many times greater than the cpm of the sample. Therefore the uncertainty of the sample cpm will not be important in the uncertainty of the efficiency.

However this method is rapid and the efficiency is measured in actual sample, without the necessity to run a series of quenched standard, but different type of quenchers will not affect the validity of this method /Hor74/. On the other hand, the sample can not recover if the internal standard is identical to the sample, the sample is not recountable. There are also certain hazards to opening up the vial and adding something extra on it /Hor74/.

2.5.2 Sample Channels Ratio (non-standard method)

A (SCR) method is a very good method of monitoring the quench effect. By monitoring the ratio of counts in two channels, it is possible to measure the amount of quench. The method does not require the addition of anything to scintillator solution, and the sample can be recounted as often as needed. The method is limited to the level of radioactivity in the sample and does not give reliable results if the quench is great. The two counting channels can be selected in several ways. This method requires a standard quench curve. A series of samples, as nearly

identical as possible with the samples to be measured, are counted which have known amounts of the radioactive nuclide and increasing amount of quenching agent. The counting efficiency and the sample channels ratio are measured for each quenched standard. The counting efficiency is plotted as a function of the sample channels ratio. Subsequently, an unknown sample is counted and its sample channels ratio measured. The counting efficiency for the unknown sample is obtained from the standard quench plot.

This method can be only used, if the counting rates of the sample are high. The quench grades are determined commonly with the help of transformed Spectral Index of the sample (tSIS) or Sample Quench Parameter of the isotope (SQP_i).

Besides, the pulse height spectrum of the measured sample is analyzed by the liquid scintillation spectrometer and outgoing of a Quench parameter, for example, this can be the canal position, on which the (SQP_i) is center of mass of the pulse height spectrum. Also this method can be used within acceptable time, only with samples of high activity. Both SIS or SQP and tSIE are used as Quench Indicating parameter (QIP's). tSIE is independent of the sample isotope and of the activity in the vial, and has a large dynamic range /Hor74/ Ste03/.

2.5.3 External standard

The most commonly used quench monitoring methods involve the use of external γ -ray sources which irradiate the solution. This method also exploits spectral movement as an indication of quenching. The known activity is not added to the sample but an external source of high energy (gamma rays) radiation placed adjacent to the vial in the counting position produces electrons in the scintillation solution due to the Compton collision process /Hor64/Tri-Carb manual/.

e.g. ^{133}Ba or ^{226}Ra , use as an external standard. The gamma rays release Compton electrons in the sample (physically the same as beta particles), which cause detectable scintillations by PMT. After summation produce a spectrum of pulse heights proportional to the Compton energy. With quenching present in the vial the spectrum is shifted toward the lower energies in the same manner as the beta spectrum of the sample radionuclide. On the basis of Compton spectrums the Quench grad of the sample can be determined. The most usual measuring for the

Quench grade is Sample Quench Parameter of the External standard (SQP_E), i.e. last point of the Compton electron spectrums and transformed spectral index of the external standard (tSIE).

It will be realized that the Compton spectrum is generated in the scintillation solution and monitors quenching in the solution. (tSIE) and (SQP_E) are based on the distribution of Compton electrons and thus unaffected by sample volume or container material. The SIE and or SQP are printed with the sample counting.

2.6 Pulse shape discrimination

The intensity of photons from a scintillation event as a function of time can be divided into at least two components, fast and slow. Fig. 2-7 /Hor74/ shows a typical intensity-time measurement. The fast component has a decay time equal to the fluorescence life time of the fluorescence solute. The slow component has decay time which is about 200-300 nsec /Bik64a/.

The total emission intensity-time equation as a function of the decay time τ_n of each component is given by the expressions 2-12

$$I(t) = I_1 \exp(-t/\tau_1) + I_2 \exp(-t/\tau_2) \dots I_n \exp(-t/\tau_n) \quad (2-12)$$

Course of fluorescence /Bir64b/ Vol68a/ Vol68b/

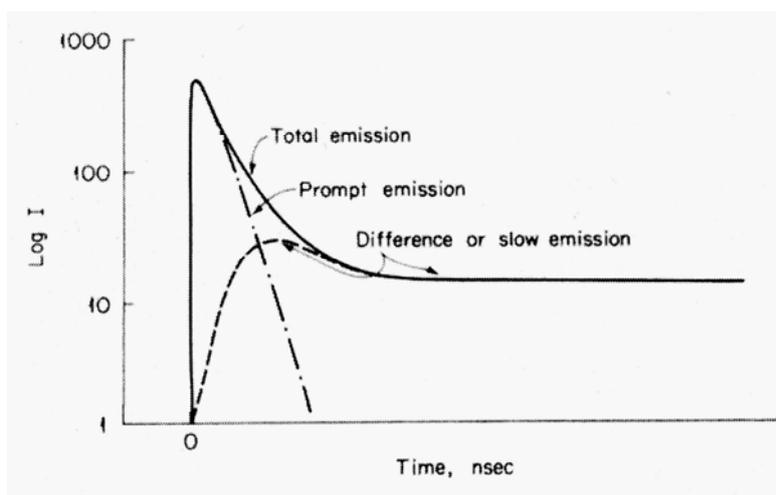


Fig 2-7: A representation of the scintillation intensity from an organic scintillator solution as a function of time showing the division of the total intensity into the prompt and slow components

Usually $\tau_1 \sim 1-3$ nanosec and $\tau_2 \sim 200-300$ nanosec are absorbed. The diffusion-controlled component has been shown to be due the annihilation of two triplet excited molecules $T_1 + T_2 \rightarrow S_1 + S_2$.

The energy transfer process results in the formation of a ground-state molecule S_0 and a singlet by excited molecule S_1 . The S_1 molecule will fluorescence with the emission of photons which are the same energy distribution as those produced directly (i.e., prompt) $S_1 \rightarrow S_0 + h\nu$

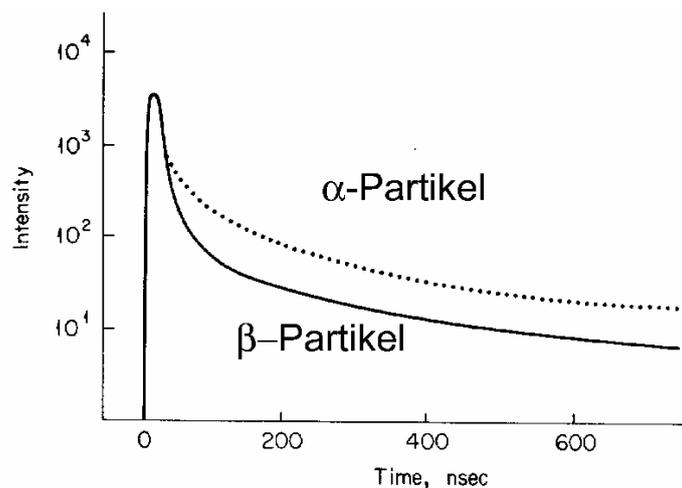


Fig 2-8: Scintillation intensity (normalized at the peak intensity) for excitation by electrons and protons or alpha particles

The main use of pulse shape discriminations to distinguish two types of particles (electron excitation in the presence of recoil protons or alpha particles) with different specific ionization which are exciting the liquid scintillators at the same time.

2.7 Structure of the measuring systems

Within the scope of this work mostly detection of ^{111}In (electron capture) and ^{109}Cd (β particles) were carried out by a LKB Wallac 1220 Quantulus and Tri-Carb®. Gamma counters are also were used to control the activities and gamma spectroscopy for real sample experiment.

2.7.1 LKB Wallac 1220 Quantulus

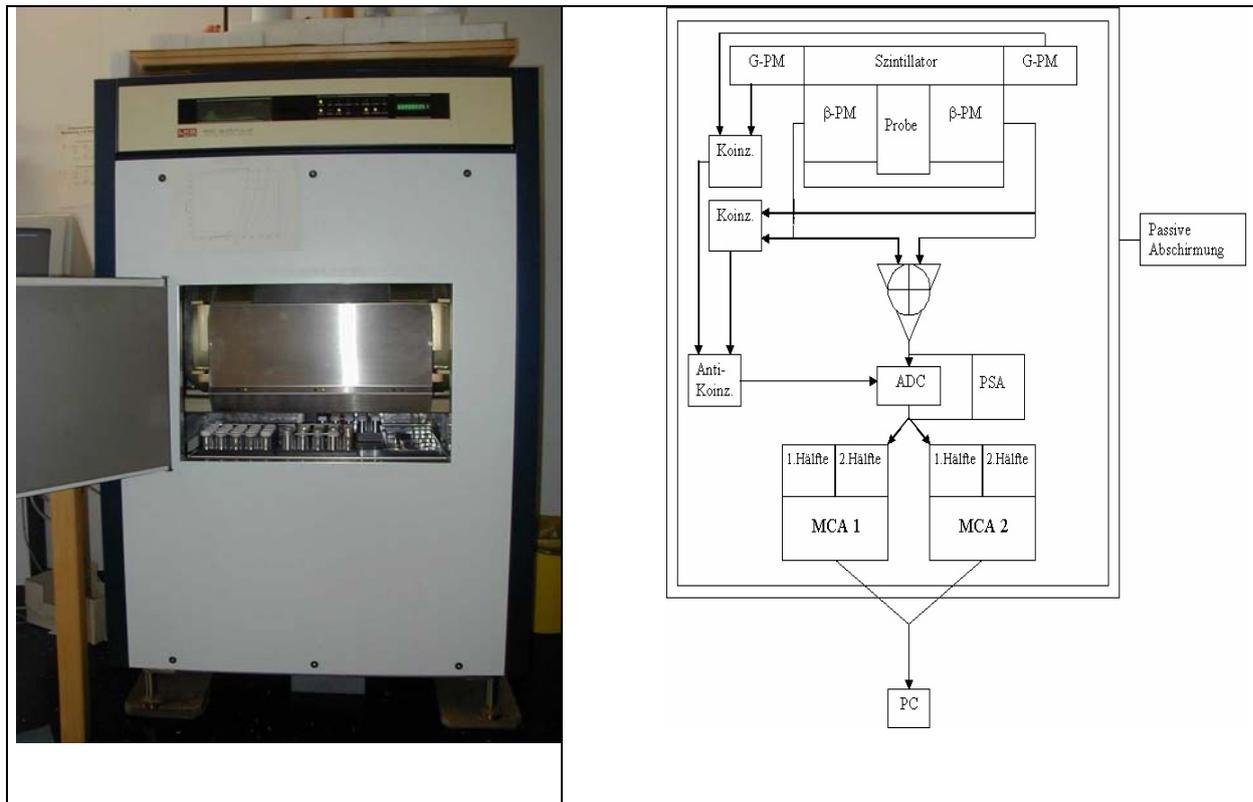


Fig 2-9: LKB Wallac 1220 Quantulus, Frontal view and schematic structure

The LKB Wallac 1220 Quantulus is appropriate for measurements very low counting rates; the background from outside radiation sources and cosmic radiation is decreased by two screens. On the one hand the Quantulus possesses a passive screen consisting of a lead layer, cadmium and copper, which absorbs or converts radiations from the outside into low-energy radiation, which does not disturb the measurement. In addition to that the Quantulus possesses an active screen. There is a tank above the sample measuring position, which is filled with liquid scintillators. This tank is surrounded by two photomultipliers (G-PMT), which is switched into the coincidence. The sample is likewise surrounded by two photomultipliers (β -PMT), which are switched into the coincidence. G-PMT and the β -PMT again are switched into the anti-coincidence. If a quantum arrives from the outside into the tank (scintillator liquid), releases a flash, is detected by both G-PMT (coincidence). Even if this quantum releases a flash in the sample, which is registered by the β -PM, then the anticoincidence circuit of the two photomultiplier systems prevents a subsequent treatment of this signal. The pulse-voltages from the β -PMT converted to an

analogue-digital converter (ADC) and a multichannel analyser (MCA). There are additional options to decreasing background from analysis (PSA) and pulse-Amplitude comparison (PAC). The Pulse Shape Analyzer (PSA), standard feature in "QUANTULUS", allows simultaneous acquisition of pure alpha and beta spectra from mixed radiations of a sample. There is a selectable threshold value so the events below this threshold are not counted (Bias) and there is a luminescence control.

The admission and storage of the signals take place at a personnel computer, using a software /Qua87/, which belongs to the Quantulus. For the treatment of the spectra the Origin software /Ori97/ was used.

Preparation of individual measuring programs permitted an automatic investigation of a large sample series and very different samples with this equipment.

2.7.1.1 Shielding

The Quantulus achieves ultra-low background levels by both passive and active forms of shielding. The passive shielding consists of a large amount of asymmetric lead block that encloses the sample PMTs. and the internal cavity surrounding the PMTs is lined with high purity copper (Fig1). A layer of Cadmium, lined with copper, surrounds the sample PMTs, to shield against neutrons (Kojola et al., 1984). The passive shield is thickest at the top, where the cosmic ray flux is most intense. Active shielding in the Quantulus is in the form of a liquid scintillation anticoincidence guard, which completely surrounds the sample phototubes, within the lead shield. This active guard has an additional pair of 'guard' PMTs, which normally operate in anticoincidence with the sample PMTs, thus rejecting cosmic induced pulses.

2.7.2 Tri-Carb liquid scintillation system

Packard's Tri-Carb meet any counting need, from basic research to environmental applications /Tha-ABA008/.

Tri-Carb liquid scintillation system (Packard, model MINAXI 4000 series) is a dual region, multi-micro-processor based multi-user units. This LSC system is designed

for quantitative detection of beta radiation, other forms of radiation, and various types of luminescence.

A printed record of all such measurements with automated sample changing, batch definition, data accumulation and a real time display of all counting results is provided by the system.

The sample capacity depends on the use of cassettes and the cassettes have been programmed to select any one of the 15 unique user programs stored in system memory.

The system consist of the major areas: scintillation detection, sample changer, spectralyzer TM, System control, program conversation and Video display.

Physically the detector consists of two opposed bi-alkali Integrated Photomultiplier Tube Assemblies (IPA) and a light-tight detection chamber, shielded by approximately 2 layer of lead to reduce the effects of external radiation which contain a reflector causes more efficient collection of light from the sample.

The SPECTRALYZER analyzes sample spectrum to provide a method of Efficiency determination. A spectral Index of Sample (SIS) is calculated and is related to the quenching of the sample.

With the external standard, the SPECTRALYZER analyzes the spectrum and produced a Spectral Index External Standard (SIE). This monitors the degree of quenching in the scintillation solution and can compensate the region for Automatic Efficiency Control /Tri84/.

2.8 Calibration curve and efficiency

A quench standard curve is performed with a series of standards in which the absolute radioactivity (DPM) per vial is constant and the amount of quench increases from vial to vial. This curve uses the relationship between counting efficiency and QIPs or (tSIE), SIS or (SQP) to correct the measured CPM (counts per minute) to DPM (disintegration per minute or absolute activity). The DPM value in each standard is known. The efficiency will calculate with the following relationship

$$\frac{cpm}{dpm} \times 100 = \%Efficiency \quad (2-13)$$

The QIPs are measured for each standard. A correlation is made using QIP on the X axis and % efficiency on the Y axis. The curve is fitted to the standard points.

Figures 2-11 and 2-12 show quench curves for ^{111}In using SIE and/or SQP as the QIP with Tri-Carb and Quantulus LSC.

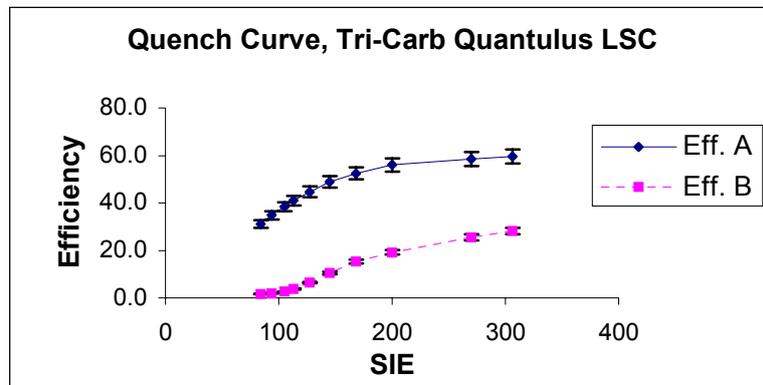


Fig 2-11: The counting efficiency for ^{111}In as a function of SIE for channels A (0-400) and B (0-2000) at Tri-Carb

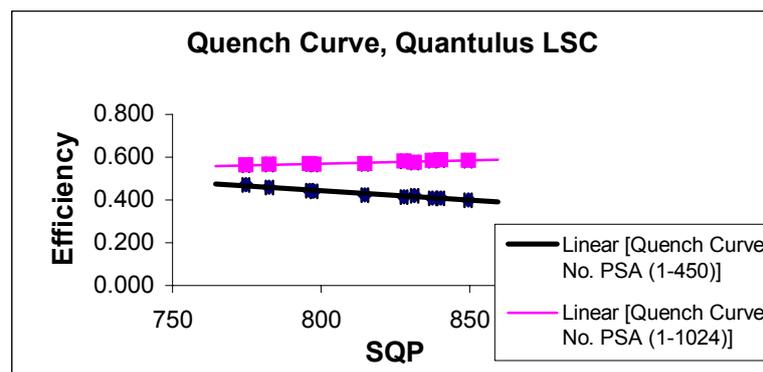


Fig 2-12: The counting efficiency for ^{111}In as a function of SQP for channels A (1-450) and B (1-1024) Quantulus LSC

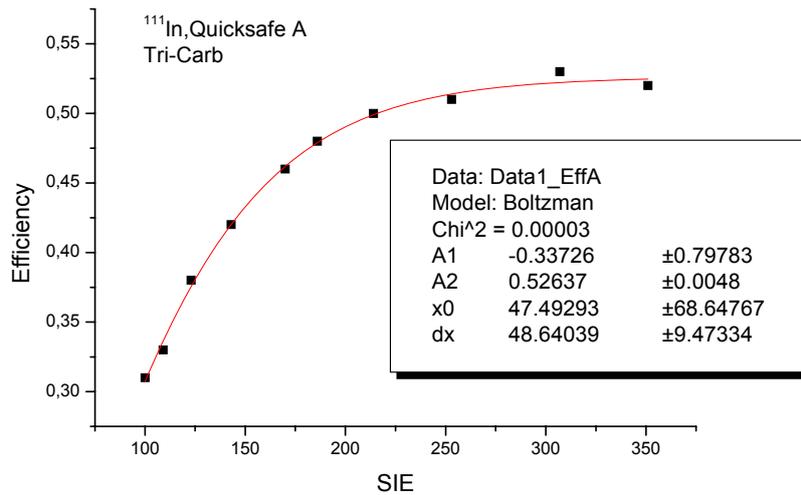


Fig 2-13: Calibration curve for ^{111}In using Quicksafe A cocktail at Tri-Carb LSC

Fig. 2-13 illustrate that in order to be able compute the efficiency for samples with other SQP(E), a Boltzmann function was used to determine the efficiency.

2.9 Gamma spectrometry

In this work γ spectrometry was used briefly to check the activities of samples and also was used counting the activity of the separation fractions in real sample experiment at JFZ. The methodology is explained on the following page.

The diagram below shows the schematic structure of the used high pure-germanium detector.

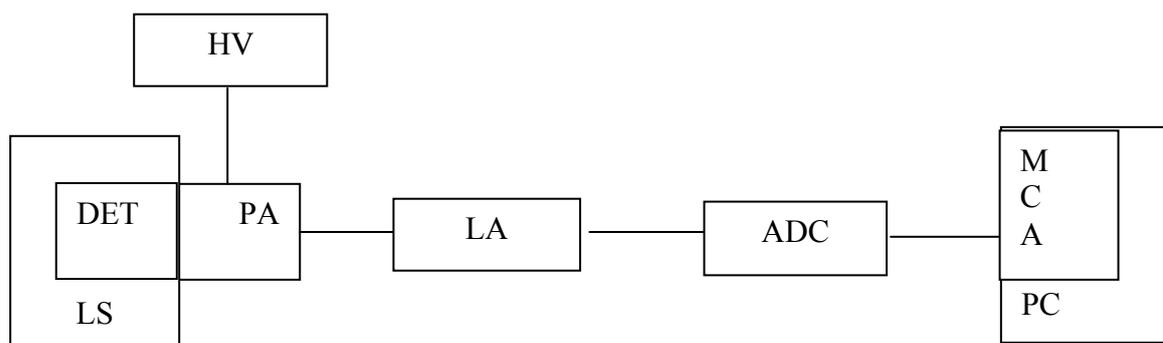


Fig 2-14: The schematic structure of the high pure gamma detector.

Where:

LS, is a passive screen (lead shielding).

DET, is a High pure germanium detector.

HV, is the high voltage power supply.

PA, is the Preamplifier.

LA, is the linear amplifier.

ADC, shows the analogue to digital converter.

MCA, is the multi channel analyzer.

PC, is the personal computer.

The detector was settled inside a passive screen from lead to reducing the background. The detector (DET) consisted of a high pure germanium crystal, which was cooled with liquid nitrogen. A high voltage was applied to the detector, which made possible separation of the pair of charges developing in the detector. The number of pair of charges depends on the absorption of (quantum energy of gamma rays) delivered energy to the germanium crystal.

The preamplifier converts the ionization charge developed in the detector during each absorbed nuclear event to an output pulse whose amplitude is proportional to the total charge accumulated in that event. The pulse decays exponentially with a time constant in the order of $< 50\text{ms}$ (nominal) to segregate successive events in high count rate applications. The impulse was passed through the linear amplifier (LA), strengthened and in the form of process able brought to the analogue-digital converter (ADC). The digitized signal was led to the multichannel analyser (MCA). The admission and storage of the signals took place at a personnel computer with the using of the target software /Tar91/. Evaluation of gamma spectra carried out from gamma w software /Wes96/Hap03/.

During experimentation with real sample at JFZ, gamma ray spectrometry was done using a high purity germanium detector (HPGe) with a relative efficiency of 30 %. The measuring geometry was 50 cm and 10 cm distance.

The detector was connected to an AMETEK-ORTEC multichannel buffer (919) and the software "Gammavision" (ORTEC) was used for data acquisition and spectrum analysis.

3 Experimental

Since data regarding the behaviour of Indium and Cadmium on the four Solid Phase Extraction (SPE) materials are not available, distribution coefficients D_w under a variety of different conditions have to be determined in order to find the conditions best suited for Indium-separation, chemical purification and Cadmium-recovery. The parameters to be varied include: different types and concentrations of acids and the concentration of different complexing agents and/or other salts added to the eluent. In order to verify the suitability of the identified optimum conditions appropriate eluent volumes have to be evaluated by elution-studies. Finally decontamination factors (DF) and recoveries (R) have to be determined.

The separation methods depend on the type of target used for the production of ^{111}In . In a large scale production, the irradiation is carried out internally on Ag or Cd targets usually electroplated onto a copper support are used. Often an inert material like Rhodium/gold is placed between the support and target material /San96/.

The solution of the dissolved target (by etching and or dissolving) contains the radioindium to be separated as well as differing amounts of supporting material, in most instances copper.

The radiochemical separation procedures should be capable of handling this situation /San96/.

3.1 Materials and methods

3.1.1 Reagents

The following chemical solutions were used in this work; Nitric, hydrochloric and sulphuric acid were prepared from the (p. a) analytical grade. All other chemicals and reagents were of analytical grade and used without further purification.

Deionised and purified water (18 M Ω) from a Milli-Q50 water purification system was used. (Fa. Millipre, Billerica, Ma, USA)

All used Scintillation cocktails (Optiphase HiSafe 3, UltimaGold AB and Quicksafe scintillation cocktail) were purchased from Perkin-Elmer Life & Analytical Science Company (Boston, MA, USA).

The solid phase extraction materials (loose material, packed columns and cartridges) came from the Eichrom Technology's company (Darien, IL, U S A)

The ^{111}In -chlorid was from TYCO Healthcare GMBH (Mallinckordt Medical B.V. Holland) and ^{109}Cd radionuclide was from (American international PLC) for all other standards refer to chapter 4.

Cd-foil (Good fellow, 99.999%) of natural isotopic composition (Fa. ChemPur Feinchemikalien und Forschungsbedarf GmbH, Karlsruhe).

3.1.2 Devices

Liquid scintillation spectrometers used were a LKB Wallac 1220 Quantulus from Perkin-Elmer Life & Analytical Science Company (Boston, MA, USA) and/or a Tri-Carb® 4000 Series Liquid Scintillation System, from Pacard Instrument company, INC. The γ -spectrometers from different companies were used: Ortec (AMETEK, Paoli, PA, USA), Tennelec (Canberra, Meriden, CT, USA) and Traget (Köln, Germany). The centrifuge equipment was from Otto E. Kobe Company, and the shaker from Heidolph Company.

The counting containers (vials), both; PE (poly vial 20), as well as the glass counting containers (Wheaton k-poor glass) were acquired from Zinsser (Frankfurt, Germany). The spectroflame P were used for ICP-OES from Analytical Instrument, Germany. Empty 2 mL Polypropylene columns (0.8 cm highest without hydrophilic frits) were acquired from Eichrom ompany (Darien, IL, USA).

For batch experiments (extractions) 2.5 mL reaction containers were used from Eppendorf (Hamburg, Germany).

Transfer pipettes, came from Fisher Scientific (FisherBrand, Schwerte, Germany) and/or Eppendorf (Hamburg, Germany). The expendable materials such as one-way pipettes (3mL and / or 10mL), PE-vials and beakers were acquired from Roth (Karlsruhe, Germany) and VWR (Frankfurt, Germany). A Finn tip stepper disposable

syringe was from Thermo lab System (Helsinki, Finland). The bond elutes reservoirs, filtration equipments, (Reservoir-2 frits, 12mL capacity) were used from Varian company (Middleburg, The Netherlands).

High pure water was received from a MilliQ50 plant (Millipore Company, Billerica, MA, USA).

3.2 Solid phase extraction materials

As discussed in chapter one, solid phase extraction (SPE) is generally used for different separation methods. Solid-phase extraction (SPE) combines the high selectivity of LLE methods with the ease of handling of IEC-methods /Die99/.

The solid-phase consists of a supporting inert polymer, organic or inorganic, on which a highly selective extracting agent, often derived from experiences with LLE separations, dissolved in an organic diluent, is adsorbed /Pai01/ Zai90/.

Due to their high selectivities and fast kinetics SPE materials allow the use of small columns and high flow rates, thus saving operating time is achieved.

Four different SPE-materials are likely to be useful for Indium/Cadmium separations, in this method; TEVA, TRU, Ln and Ac resins.

3.2.1 TEVA Resin®

TEVA® Resin (TEtra Valent Actinide Resin /Hor95/) consists of Aliquat-336® sorbed on a polymeric support. The separation is based on of anion exchange extraction, the basic structure is shown in Fig 3-1 1 /Eic99-00/ Hor00, 95/.

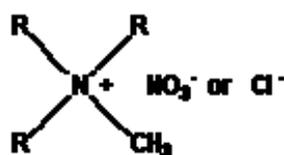


Fig 3-1: Trialkylmethylammonium nitrate (or chloride)



Aliphatic quaternary amine is the active component of this resin. It has properties similar to those of typical strong base anion exchange resins. However, because the

functional groups are in a liquid form, rather than fixed to a polymer backbone (as with IX resin) these groups have greater flexibility to coordinate around target anions. This means that the uptake of these ions is generally higher and often at lower acid concentrations /Eic00/.

This behaviour is shown in Figures 2 (left and right), which are the acid dependency curves of TEVA Resin for the actinides and technetium from nitric and hydrochloric acid. Tetravalent plutonium, neptunium and thorium show maximum uptake in the region of 2 M to 4 M nitric acid. The decrease in k' for the tetravalent actinides as nitric acid concentrations greater than 2-4 M is due to competition from nitrate anions for complexation sites on the resin. k' is related to the liquid-liquid distribution ratio (D) and it can be calculated from the number of free column volumes to peak maximum /Hor92/.

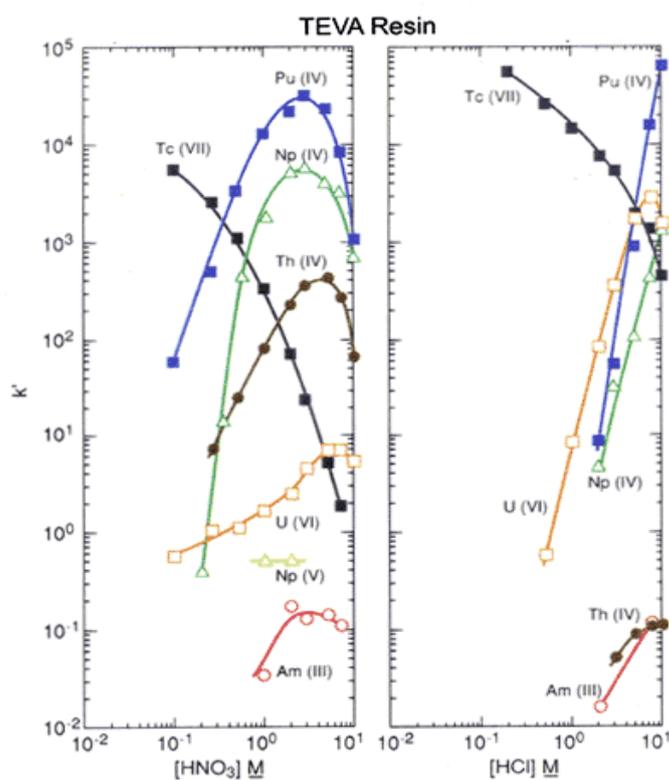


Fig 3-2: Acid dependency of K' for various ions at 23°C /Hor95/.

Horwitz et al. reported the data in Figures 3-2 from studies performed with experimental batches of TEVA Resin. The y-axis, k' , is a measure of uptake, corresponding to the number of free column volumes (FCV) to peak maximum in a chromatographic column.

The differences in the uptake curves for nitric and hydrochloric acid can be exploited to separate certain actinides from each other. For example, all the tetravalent actinides can be loaded from 3M nitric acid. Valence adjustment may be required to assure that the actinides are tetravalent. Then, by switching to 6M HCl, Th (IV) can be selectively eluted while Pu (IV) and Np (IV) remain on the column.

Although not shown on Figures 3-2, neutral, and even basic solutions, show a strong uptake of technetium. Work performed by Darrin Mann's laboratory at K-25 in Oak Ridge demonstrated It was also shown that, Aliquat-336[®] is a very suitable component for preconcentration of Indium and the removal of Iron and Copper impurities originating mainly from the backing of irradiated targets /Ne166/Koi77/Nis98/. Eichrom TEVA Resin[®] is available in three particle sizes (100-150 micron, 50-100 micron, and 20-50 micron), in the bottle sizes or prepacked in slurry packed 2mL columns, 2mL dry pack cartridges, and 47mm discs.

3.2.2 Organophosphorus chelating agents

It has been suggested that organophosphorus chelating agents might be useful for the selective extraction of Indium /Ne166/Koi77/Raj94/. TRU Resin[®], Actinide-resin[®] and DIPEX Resin[®] were chosen for this study, since all of them are comprised of such chelators. In addition it is known that TRU Resin[®], DIPEX Resin[®] and Ln Resin[®] preferably extract trivalent cations even in the presence of a large excess of other divalent cations, which will certainly enhance the quantitative Indium/Cadmium separation.

3.2.2.1 Actinide Resin[®]

Actinide Resin[®] is based on the DIPEX[®] Extractant, PP-di (2-ethylhexyl) methane-diphosphonic acid (H₂DEH [MDP]) the basic structure is shown in Fig. 3-3. As shown in Fig. 3-4 the resin exhibits an extraordinarily high affinity for the actinide elements.

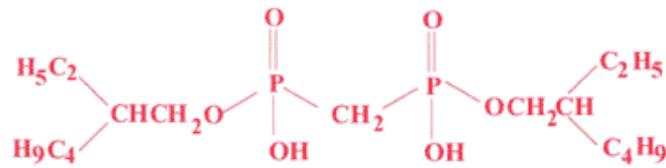


Fig 3-3: DIPEX extractant

For acid concentrations less than 1M (especially for HCl), the retention of actinides is dramatically higher on Actinide Resin than on TRU-resin®. This makes the resin quite useful for the preconcentration of actinides out of large volume aqueous samples.

In fact the resin is ideal for monitoring actinides in aqueous discharges For a very rapid analysis, the resin may be exposed with the sample in a batch mode and then measured directly by liquid scintillation /Hor97/.

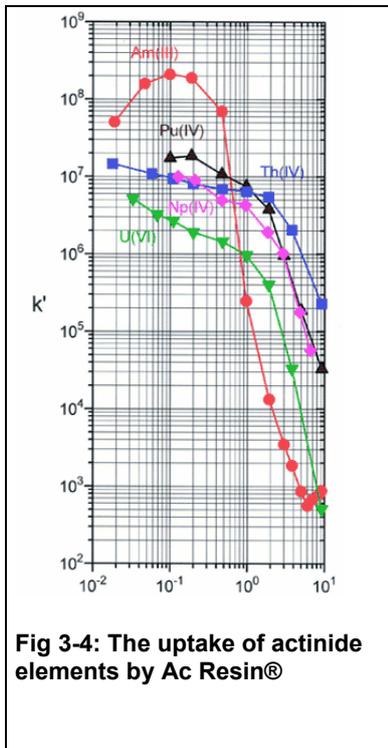


Fig 3-4: The uptake of actinide elements by Ac Resin®

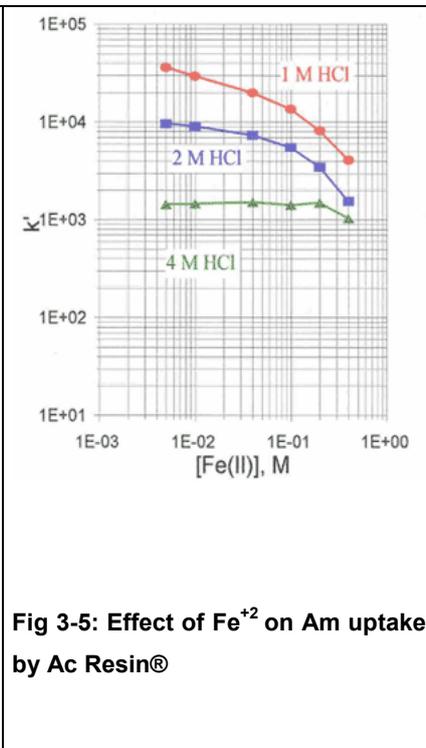


Fig 3-5: Effect of Fe⁺² on Am uptake by Ac Resin®

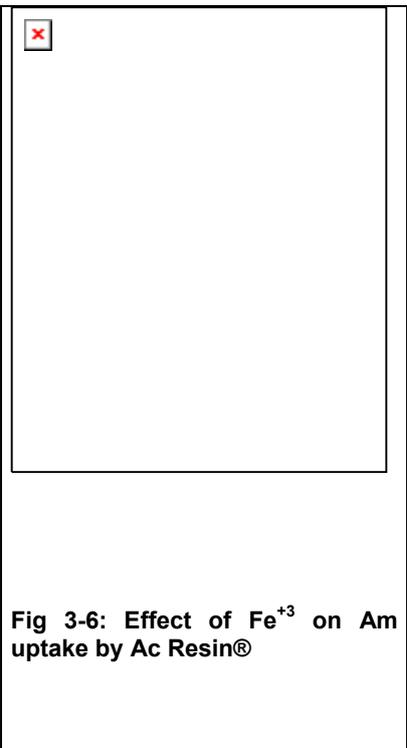


Fig 3-6: Effect of Fe⁺³ on Am uptake by Ac Resin®

Fig. 3-4 shows the capacity factors of selected Actinide element for Actinide Resin® on different hydrochloric acid concentrations, Fig. 3-5 shows the capacity factor of Am⁺³, on Actinide Resin® for different Fe⁺³ concentrations, and Fig. 3-6 shows the

Capacity factor of Am^{+3} on Actinide Resin® for different Fe^{+2} concentrations /Eichrom home page/ The effect of iron on the retention of the actinides is often a concern in radiochemistry. Figure 3-5 and 3-6 demonstrate the effect of Fe^{+3} and Fe^{+2} on the retention of Am^{+3} in a variety of HCl solutions. While the effect of ferric ions (Fe^{+3}) is significant, the effect of ferrous ions is negligible. In samples with suspected high concentrations of iron, the addition of a reducing agent, such as ascorbic acid, will minimize the effect of iron on the retention of americium.

Actinide-resin is available as a 100-150 μ resin and is sold in bottles or ready to use in prepacked columns for gravity flow investigations.

3.2.2.2 Ln Resin®

Ln Resin is also grown out of the transformation of a selective organic extractant into an extraction chromatographic resin. The extractant used in the Ln-resin® is di (2-ethylhexyl) orthophosphoric acid (HDEHP) Fig. 3-7 /Hor75/.

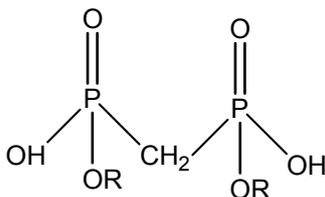


Fig 3-7: Ln Resin® extractant

The data reproduced in Fig. 8 by Horwitz et al. (1995), has been used as the starting point for a number of radiochemical separations in use today. Ln Resin has been applied to the analysis of radium, neodymium, and promethium and as the data in Fig.8 might indicate, many more analytical applications are possible and may already be operational /Hor75/.

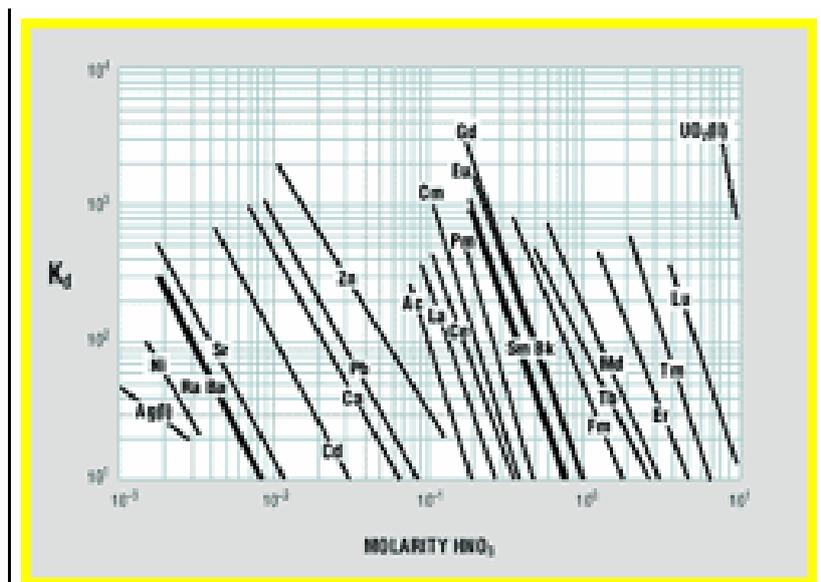


Fig3-8: Uptake of various elements by Ln Rsin® /Hor75/

Early work by Horwitz et al., provided distribution coefficients (K_d) versus nitric acid for various metal ions using HDEHP on a hydrophobic support. This data is reproduced in Fig.3-8 and has been used as the starting point for a number of radiochemical separations in use today. Note that for Eichrom's Ln Resin®, K_d can be converted into k' (an approximation of free column volumes to peak maximum) by dividing by 4.33. Ln Resin® has been applied to the analysis of radium, neodymium, and promethium and as the data in Fig. 3-8 might indicate, many more analytical applications are possible and may already be operational. Ln Resin® is manufactured in three particle sizes (20-50 μ m, 50-100 μ m, and 100-150 μ m) and is sold in bottles or ready to use in prepacked columns (for gravity flow) and cartridges.

3.2.2.3 TRU Resin®

The TRU Resin® (Trance Uranium Resin, /Hor93/) is based on the extractant system consisting of octylphenyl-N,N-di-isobutyl carbamoylphosphine oxide (CMPO), dissolved in tri-n-butyl phosphate (TBP) Fig. 3-9 and CMPO molecule is shown in Fig. 3-10 /Hor93/.

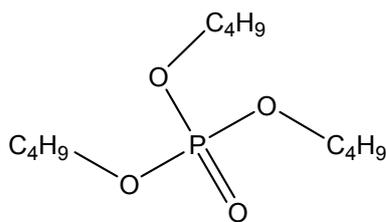


Fig 3-1: The structure of TBP

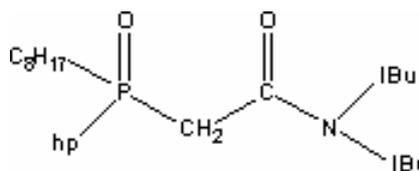


Fig 3-2: The CMPO molecule (carbamoylphosphine oxide)

The CMPO/TBP solvent system complexes actinide elements and can thus extract them out of certain aqueous solutions.

The bed density of TRU Resin® is approximately 0.37 mg/mL, with a working capacity of 2 mg Am per mL of resin or 4 mg Am per 2mL pre-packed column. This value represents 20% of the theoretical maximum loading capacity of the resin.

TRU Resin® is manufactured in three particle sizes (20-50µm, 50-100µm, and 100-150µm) and is sold in bottles or ready to use in prepacked columns (for gravity flow) and cartridges (for vacuum assisted flow /Hor93/95/97/).

All of the extraction materials show limited loading capacities of very few mg of ions per mL resin. Therefore finding conditions that allow the selective extraction of Indium is crucial since it has to be separated from the presence of a large excess of Cadmium. As it can be seen in the course of this work, (SPE) method with the use of TEVA Resin®, Actinid Resin® and Ln-resin® is a fast and convenient way for further in-hospital purification of ¹¹¹In solutions shortly before its use for medical purposes.

All the extraction-materials in this work were from Eichrom technologic system, as discussed in this chapter, extraction chromatography (EXC) is a technique that is ideally suited to the separation of radionuclides from a wide range of sample types. This technique combines the selectivity of liquid-liquid extraction with the ease of operation of column chromatography. Table 1 lists a number of EXC resins that we are worked on them and they are manufactured by Eichrom technologies company.

Table 3-1: Chromatographic resins from Eichrom Technologies

Material	Selectivity	Particle size	Extractant agent
TRU Resin	actinides (111, 1V, V1), Ln (111)	100-150µm	CMPO/TBP
TEVA Resin	Th(1V), Np(1V), Pu(1V), Tc(V11),Am	100-150µm	Trialkylmethylammonium nitrate (or chloride)
Ln Resin	Ln(111)	100-150µm	Di(2-ethylhexyl) orthophosphonic acid(HDEHP)
Actinide Resin	actinides	100-150 µm	P,p'-di(2-ethylhexyl) methanediphosphonic acid

3.3 Separation procedures and methods

The separation of radioindium from macro amounts of Cadmium is developed from a procedure based on the known coefficients of Indium and Cadmium ion distribution between SPE-materials and appropriate acid solutions /Zei89/Gel04/.

Weight distribution ratios (D_w values) are determined, using batch techniques, namely by exposing weighted amounts of SPE materials (or prepacked columns) with ^{111}In and or ^{109}Cd solutions with known volumes and known activities (under various mixing conditions) for one hour. D_w values are calculated from the measured activity of the aqueous phase after removing the solid phase by means of filtration and or centrifuging methods, using the following equation /Hor97/.

$$D_w = \frac{(A_0 - A_S)}{m_{\text{resin}}} \cdot \frac{V_{\text{liquidphase}}}{A_S} \quad (1)$$

A_0 = activity before extraction

A_S = activity after extraction

m_{resin} = amount of resin (approx. 0.01 g)

$V_{\text{liquid phase}}$ = volume of liquid phase (1.1 mL)

Elution-studies are carried out by loading known activities of ^{111}In or ^{109}Cd on prepacked columns and in case of the TEVA[®]-material also commercially available discs. Elution curves are obtained by adding appropriate aliquots of acid solutions of known concentration and subsequent determination of the activity of the eluate fractions.

Cadmium decontamination factors are determined by loading known, high activities of ^{109}Cd on the column or disc. Afterwards the separation is performed and the Cadmium activity in the Indium fraction is measured. The decontamination factor is calculated by:

$$DF = \frac{A_0}{A_S} \quad (2)$$

The same experiment is performed with known activities of ^{111}In to determine the Indium recovery (R_{In}):

$$R_{\text{In}}[\%] = \frac{A_S}{A_0} \cdot 100 \quad (3)$$

The Indium separations and Cadmium recoveries were determined analogous using ^{111}In and ^{109}Cd standards. Furthermore the influence of high amounts of Cadmium on the Indium extraction was examined for the Ln-resin[®], Ac Resin[®] and TEVA Resin[®]. The results and discussion are presented in the following chapter. The influences of some inactive trace contaminations (Fe, Al and Cu) on the separation were determined measuring their concentration in the ^{111}In fractions by inductively coupled plasma-optical emission spectrometry (ICP-OES) and/or AS /Pro00/Sal00/.

3.3.1 Determination of weight distribution (D_w) and decontamination factors (D_f)

In order to find the conditions best suited for the $^{111}\text{In} / ^{109}\text{Cd}$ separation, D_w -values for ^{111}In and ^{109}Cd and decontamination factors (D_f) for ^{109}Cd in the Indium fractions, were measured for the different SPE materials by exposing a weighed portion of

resin with a measured volume of acid solution of appropriate concentration (100 μ L of radioactive Indium and Cadmium solutions added to each sample) for 75 minutes under various mixing conditions. These included different acids (H_2SO_4 , HCl, HNO_3 , and HBr), additives (such as NaBr and NaCl) and complexing agents such as EDTA and mixtures of them.

The calculations were carried according to equations 1 and 2 with A_0 and A_s representing the activity of aqueous phase before and after equilibration with the resin /Hor 92-97/Chi98/.

3.3.1.1 Sample preparation

The sample preparation was accomplished by two different methods; filtration and centrifugation.

a) In case of the filtration method sample preparation included several steps;

1-10 mg of a special-resin were weighed into a plastic micro tube (2.2 mL volume Eppendorf). Each elution study was repeated 13 times.

2-1mL of the appropriate acid (at concentrations between from 0.001 to 10 M) was added.

3-The samples were shaken for 15 min.

4-100 μ L of the ^{111}In or ^{109}Cd standard solutions was added.

5-Each sample was shaken for 60 min.

6-In order to separate the resin from the bulk of the solution, the combined solutions were passed through a suitable filter (Varian Bond Elute Reservoir 12 mL). The residue solution of each experiment was collected in a glass and or a plastic scintillation vial (20 mL volume).

7- The Eppendorf were washed one more time with 1ml of appropriate acids and through out again on the filters (collect into the said vials (at 6 stage).

8-2 mL deion water were added to each samples.

9- Filtrated collected fractions were evaporated, to dryness and redissolved in 5mLHCl 0.1M.

10- 10 mL Scintillation cocktail was added on each sample

b) In the case of centrifuging method, which is a very rapid available method, the following stages have been done;

1-10mg resin were weighted into Eppendorf vials (2.2 mL volume), as said above.

2- 0.9 mL of the different concentrations (>0.001 up to 9 M) of appropriate acid (HCl, HNO_3 and H_2SO_4) was added to the Eppendorf vials.

3-The samples were shaken for 15 min.

4) - 100 μL of the ^{111}In or ^{109}Cd standards were added to the each vial. The activity of the radioisotopes should be in the order of 1000 to 10000 DPM/100 μL .

5- After adding the activities into the vials, the samples were shaken again for 60 min.

6-The samples were centrifuged for 10 min at the middle speed with.

7- 500 μL of the aqueous phase of the samples, were withdrawn and were pipetted into the Glass-LSC vials (20mL), then these samples were evaporated to dryness.

8-4.5 mL deion water and also 0.5 mL of HCl 0.1 M were added to the samples.

9-10 mL scintillation cocktail was added to each sample.

For determination of many of D_w and D_f values, sample preparation was done by these two methods. Similar and acceptable results were obtained for both methods; however the centrifuging method has the advantage of saving preparation time, providing easier handling and producing smaller amounts of radioactive waste.

3.3.1.2 Counting and calculations

To avoid quenching problems, the cocktail must be checked for phase separation prior to measurement. Solutions must be homogeneous, transparent and colourless. Therefore after adding the cocktail to the sample, the vials were shaken until aqueous and organic phase were mixed completely. Afterwards the cocktail solution is cooled to a temperature of about 10⁰C in a refrigerator /Eik09/. Liquid scintillation spectrometry LSC (Using the Tri-Carb or LKB Wallac 1220 Quantulus) was used to measure the samples.

The following standard measurement conditions were selected for all experiments. Using the Tri-Carb (LSC), 10 minutes counting time were chosen (cpm) for identification. Using the Quantulus (LSC) 5 minutes for each sample and an extremely high counting interval (60-600 minutes) sufficient for the evaluation of the background (BG) count rate were used for measurements. The determination of D_w-values and D_f-factors were carried out from the following equations.

A₀, the activity before extraction, (calculated activity) is calculated from equation 4:

$$A_0 = A_t(0.1)EXP(-Ln(2)*t/T_{1/2}) \quad (4)$$

Where:

t, is the reference time and 0.1(mL) is the amount of ¹¹¹In or ¹⁰⁹Cd radioisotopes contacting as a batch in each sample.

A_t, is the activity of the standard at reference the time t.

A_s , is the activity of the samples after extraction (measurement activity), which can be calculated by equation 5.

$$A_s = \frac{cpm(\text{exp}) - cpm(\text{BG})}{(60) / E} \quad (5)$$

Where:

Cpm (exp), is the count per min for each sample obtained from LSC.

Cpm (BG), is the background counting obtained from LSC.

E, is the efficiency of LSC for special radioisotope.

The efficiency is derived out from the Boltzmann equation (6), which is explained in chapter 1.

$$Y = \frac{A_1 - A_2}{1 + \text{Exp}(x - x_0) / dx} + A_2 \quad (6)$$

Where:

A_1 and A_2 are the In-fit constants.

Repeatability of two subsequent measurements was excellent. For results and discussion refer to chapter 4.

3.3.2 Elution study

Elution-studies are carried out by loading known activities of ^{111}In or ^{109}Cd on to packed, prepacked, and or mini cartridge packed columns and in case of the TEVA-material, commercially available discs.

Elution curves are obtained by adding 5 mL aliquots of acid of known concentrations and subsequent determination of the activity of the eluate. The percentage recoveries of ^{111}In and ^{109}Cd radioisotopes (R_{In} (%) and R_{Cd} (%)) were determined by equation (3).

All experiments are repeated 2 or more times, therefore the average values for all experiments are calculated.

The elution behaviour of Indium and Cadmium cations on the TEVA Resin®, Ln Resin® and Ac Resin® column were evaluated using procedures described in /Hor92-95/. The columns containing known activities of ^{111}In and /or ^{109}Cd , were rinsed with appropriate acid concentrations and then stripped of radioisotopes with appropriate solutions such as particular acid concentrations, complexing agents (EDTA), and/or water.

3.3.3 Column characteristics and preparation

In most of the elution studies with Actinide Resin® and Ln Resin® in this work, columns were packed freshly by slurring the appropriate resin (500mg dry weight (particle size; 100-150 μm for Actinide Resin® and 50-100 μm for Ln Resin®) purified water Then defined aliquots of the slurry were transferred into a column body (an empty Eichrom column) at room temperature until the desired bed height was reached (5cm and. 42 mL). For separation or elution process, flow rates at room temperature of roughly 0.3 ml/min were typically employed. The resin was resettled by backwashing. A layer of frittes was placed on top of the resin to prevent disruption of the bed during sample introduction.

TEVA Resin® is used in two particle sizes:

- a) A size of 100-150µm was used for D_w value determination and to prepare some fresh columns (500 mg dry weight) for elution studies.
- b) A size of 50-100µm prepacked in slurry in 2 mL columns and / or in 2mL dry pack cartridges was used for most elution studies and Cadmium recovery determination.

Prior to the introduction of a sample, the columns were preconditioned with 5 mL of appropriate solutions. /Hor91-95/Chi98/. All experiments with these columns were repeated for 2 or more times with only small deviations in the results.

An available particle size of 50-100µm for the TRU Resin® were used for the determination of D_w .

3.3.4 TEVA Resin® experiments

As expected from literature /Lim98/Eij97/Lev73/ Indium and Cadmium show very high distribution ratios in the presence of high concentrations of chloride or bromide. According to the nature of the extractant used in the TEVA Resin®, namely Aliquat-336®, complexes with bromide (a very soft Lewis acid) are extracted preferably compared to the chloride complexes. Furthermore the results show that in general Cadmium has higher distribution ratios than Indium. Also taking into consideration the limited capacity of the disc, a separation of Indium from macro-amounts of Cadmium is very difficult, if not impossible, since both cations compete for the same free active sites.

The experiments to obtain D_w values were continued with TEVA Resin® in different concentrations of H₂SO₄, HBr and HNO₃, along with salt additives, for example different concentrations of NaCl and NaBr, with the required acids (HCl, HNO₃ and H₂SO₄). All details are listed in chapter 4.

3.3.4.1 TEVA Disc experiment

A combination of the TEVA-extraction discs and HCl might very well be suited for removing Cadmium impurities from Indium solutions, namely amounts that are well below the capacity of the disc. In order to find conditions that allow Cadmium/Indium separation, elution-studies were performed using different HCl concentrations.

Elution studies for In and Cd radioisotopes were performed as follows:

The TEVA-disc is conditioned using 2 mol L⁻¹ HCl. The disc is carefully placed on the filtering apparatus and then the funnel is placed over the disc that can allow the eluent and active solutions loading on the disc. A clean and labelled beaker is positioned below the extraction disc. The Indium solution is acidified with HCl (concentration of 2 mol L⁻¹) and passed through the TEVA-disc. All of the Cadmium and most of the Indium is extracted onto the disc. By washing with 20 mL HCl (2 M), Indium is removed while Cadmium remains or is retarded on the disc. The Indium fraction is evaporated and the residue redissolved in 5mL HCL 0.1M. The resulting solution was counted in an LSC. The TEVA-disc is cleaned by washing with at least 75 mL of 0.01 mol L⁻¹ HCl.

It was found that aqueous solutions containing rather large amounts of EDTA (0.5 mol L⁻¹) as well as 0.1 mol L⁻¹ EDTA solutions with hydrochloric acid at concentrations greater than 0.1 mol L⁻¹ can be used to remove Cd from the TEVA Disc® (the results will be described in chapter 4).

3.3.4.2 The reuse of one TEVA Disc®

Cd decontamination factors (D_f) were determined ten times using one TEVA Disc®. The above described method was applied to ten ¹¹¹In solutions of known activity 100 µL.

From the obtained ¹¹¹In recoveries and ¹⁰⁹Cd decontamination factors it can be concluded that one TEVA Disc® might be used up to three times, the results are shown in chap 4.

3.3.5 TRU, Actinide and Ln resins experiments

Weight distribution values (D_w) have been determined and elution studies have been undertaken to examine the behaviour of Cadmium and Indium Isotopes on the other solid phase extraction materials (SPE), such as Ln Resin®, TRU Resin® and Ac Resin® with organophosphorus chelating agents. Batch experiments as described for the TEVA Resins were repeated three times for separation with organophosphorus chelating agents.

As can be seen later, TRU Resin® is not a good choice for Indium/Cadmium separation, instead the Actinide Resin® as well as the Ln Resin® seems to be the best suited extractant materials for $^{111}\text{In}/^{109}\text{Cd}$ Separation. The separation efficiencies of all these three resins were examined with different concentrations of H_2SO_4 , HCl and HNO_3 . Sample preparations, counting procedures and calculations were the same as those for the TEVA Resin® experiments.

Conditions were found for the Ac and Ln resins under which the difference in the D_w values were three or four orders of magnitude. It was found that the best acid for $^{111}\text{In}/^{109}\text{Cd}$ separation is HCl . Nevertheless there are also conditions that allow In elution. The TRU Resin® was not found to be suited, since differences in D_w -values were not sufficient (chap 4).

3.3.5.1 Elution study for Ln Resin® and Ac Resin®

In order to find conditions that allow high Cd decontamination combined with high In recovery, elution studies were performed with the use of Ln Resin® and Ac Resin®

The following experiments were performed:

- 1- Columns, with Ln and Ac Resin® were prepared as described in (3.3.3), using a Varian 12 ml filter as a column's body (1 mg dry resin weight has been used)
- 2- ^{111}In and ^{109}Cd standards were prepared from radio isotope standard solution.
- 3- A_0 samples were Prepared from Indium and /or Cadmium standards (100 μL radioisotopes in 5ml HCl 0.1M)
- 4- The columns were preconditioned with 5 mL HCL 0.1 M for Ln Resin and 1 M for Ac Resin consequently.
- 5- 100 μL of radioisotopes was pipetted direct on top of the prepared columns.

6- The elution study was started with washing the columns with 250 μ L HCl (0,1 mol⁻¹ L for Ln Resin and 1 mol L⁻¹ for Ac Resin).

7-The effluent solutions were collected into plastic vials (22mL volume), these fractions are named as the wash steps.

8-At least 19 wash samples were collected (19 elution steps)

9- 10 ml L S cocktail (quick safe) were added into the samples and were counted for 10 min in LSC Tri-Carb and/ or Quantulus.

10-For (BG) determination, a blank sample was counted for 60 min by LSC. (5 mL HCl, 0.1 M contain 10-15 mL LS cocktail)

11- The washing steps were continuing from wash step (No 20) then each elution step was performed with increments of 5 mL HCl (0.1 and 1 M for Ln and Ac resins respectively) until a total of 100 mL HCl was added.

The elution study which is described above, was repeated for elution ¹¹¹In and ¹⁰⁹Cd with 1 and 0.1 M HCl for Ln and Ac-columns respectively.

It will be seen later in the results and discussion that ¹¹¹In will remain on the Ln columns even when washing with a large amount of HCl 0.1 molL⁻¹, and will be stripped washing the columns with 5-10 mL of HCl 6 molL⁻¹. Nevertheless ¹⁰⁹Cd will be eluted after a relatively low amount of eluent.

All elution studies were performed and repeated with small freshly packed columns (500mg weighed dry resins, at a flow rate of 2-3mL/min).

3.3.6 Influence of inactive Cadmium in separation

As explained in chapter 1, ¹¹¹In is produced from irradiated ¹¹²Cd and or natural cadmium) targets from the reaction ¹¹²Cd (p, 2n)¹¹¹In in a cyclotron. After a suitable "cooling" period, targets must be dissolved in appropriate acids for separation and purification procedures and purposes. However the final solutions then contain a large amount of inactive cadmium and other metal trace impurities. In order to purify the radioindium product, completely acceptable for medical purposes, it is desirable to reduce the cadmium concentration and remove other impurities. In this study the D_w values experiments and an elution study were performed as described below, to evaluate the clean-up capabilities of the method developed.

3.3.6.1 Dw determination

To determine the influence of macro amounts of Cd on the ^{111}In D_w values, several experiments for the determination of D_w values for ^{111}In were performed to find the best HCl concentration, using Ln and Ac resins. The samples therefore contained different concentrations of inactive Cd. The experiments are described below.

3.3.6.1.1 Sample preparation and procedure

1- Different concentration from of a suitable salt of Cadmium, " $\text{CdCl}_2 + \text{H}_2\text{O}$ " (0,1, 10, 50 and 100 mg mL^{-1}) were prepared in HCl 0.1 and 1 molL^{-1} for Ln and Ac resins respectively.

2-10mg resin (for Ln and Ac resins, each one 15 times) were weighted in Eppendorf vials (2.2 mL volume).

3- The ^{111}In and ^{109}Cd standards were used with the specification shows at table 2, (table 2). A_0 samples were prepared from these standard solutions.

4-The experiments have to be continued as other D_w experiments (each inactive Cd, concentration were examined in three times).

Table 2: Radionuclides standard

Nuclide	Provenience	Avtivity/ MBq mL^{-1}
^{111}In	TYCO Healthcare GMBH	333-407
^{109}Cd	American international PLC	39

3.3.6.2 Elution studies

The recovery (in % (R)) of ^{111}In standard samples, considering the last washing steps in the elution study (3.3.5.1) with HCl (6 mol/L), was determined with different

amounts (0.1, 1, 10, 50 and 100 mg mL⁻¹) of inactive Cd present in the sample in order to evaluate the influence of this macro component in the separation procedure.

3.3.6.2.1 Sample preparation and procedure

Sample preparation and procedures included several steps:

1- 10 columns were Prepared (as described in 3.3.3) (for each concentrations, in duplicate) for Ln resin and Ac resins.

2- the columns were Preconditioned with 5 mL HCl 0.1 and 1 molL⁻¹ for Ln and Ac resins respectively. 3-100 μ L ¹¹¹In was pipetted into plastic vials contains 5 mL HCl (appropriate concentration for Ln and Ac-resin).

4- The active solutions described at 3, were loaded on the preconditioned columns (no need to count this step).

5-The columns were washed two times with 5 mL HCl 0.1M for Ln and 1 M for Ac resin, (no need to count this step also).

6-The columns were washed with (5-10) mL HCl 6 molL⁻¹ to stripping the columns from radioindium. These steps were collected into the glass vials (22 mL volume).

7-In order to avoiding quenching effect (especially chemical quenching, the last wash step solution (washing with HCl 6M) was evaporated, and the dry residue was dissolved in 5 mL of HCl 0.1 M.

8-10 mL SC (scintillation cocktail) was added into the sample.

9-In order to avoid thermo luminescence and/or chemo luminescence effects, the samples should not have in a white milk-like state. Therefore, samples were kept in the refrigerator for an hour or longer.

10-The samples were counted for 10 min in Tri-Carb LSC and/or 5 min in Quantulus LSC.

11-The recovery (R_{in}) in % were overcome with the data regarding on the excel program.

All above steps have been repeated with adding inactive Cadmium solutions (concentrations of 1, 10, 50, 100 mgmL⁻¹) into the samples. It will be shown later in chapter 4, that the influence of the macro amount of inactive Cd is not be a problem in ¹¹¹In recovery.

3.3.6.2.2 ¹⁰⁹ Cd decontamination factor (D_f)

The determination of the D_f-factor for Ln Resin® and Ac Resin® in case of different concentrations of inactive Cadmium in 0.1 and 1 M HCl for Ln and Ac resin respectively, has to be done by measuring the Cd contamination in the ¹¹¹In breakthrough samples. The procedures were the same as for the other D_f determinations in this work. The decontamination factors were high enough. (Chapter 4 shows the results and discussion).

3.3.7 Possibility of reusing the same column

To show whether the Ln or Ac columns could be used more than once, an elution study was performed with one Ln and/or Ac resin. After collecting the last fraction (with 5mL HCl 6M), the columns were rinsed with 5 mL HCl 6 M again and then with 5-10 mL deionised water. The columns again were reconditioned with appropriate acid concentration. Then the columns were used for next In-recovery experiments, up to 10 times. The results are shown in the next chapter. It will be shown that each column can be reused 7 times.

3.3.8 Extraction of several inactive metal traces

For a cleanup of the radioindium product completely acceptable for medical purposes, the extraction of some commonly associated metal ions namely Cu, Al and Fe present from irradiated cadmium targets and/or target holders (Copper holder) have also been investigated for Ac Resin® and Ln Resin®. Based on the partition data the conditions for the separation of ¹¹¹In from the mentioned metal ions were identified. The separation conditions, thus developed, have been utilized for the separation of Indium from Cu, Al and Fe blends.

The elements above were mixed with the etched solution containing radioindium. The resulting solutions were loaded onto the desirable columns and eluted as

described above (3.3.6.2). The influence of Fe(II) on Ac, Ln and TEVA resins, were examined by reducing Fe^{+3} by adding ascorbic acid /Hor92/.

In previous ^{111}In separation investigations, literature studies shows that a large amount of Cu might be an important problem for Indium extraction /Mal96/, therefore in this work we are performed several elution profiles and extractions with large amounts of metal contaminations, such as Fe, Al and Cu with SPE-materials to identify the In-recoveries (R_{In}) in % of our method.

3.3.8.1 Metal trace analysis by ICP-OES

Chemical extractions and purifications of ^{111}In from inactive metal impurities were performed by several elution studies. The quantitative measurements of the concentrations of the trace elements were accomplished via one of the major techniques of elemental analysis at the faculty of chemistry of the Philips University of Marburg by the working group of Prof. Seubert analytical chemistry department Marburg University by "Inductively Coupled Plasma Optical Emission Spectroscopy "ICP-OES" (in the case of Ac and Ln resins). All the samples were prepared in two individual separation steps and the average values were calculated.

3.3.8.1.1 Sample preparation and procedure

1- Ln and Ac columns were prepared as in (3.3.3).

2- Solutions containing 1mgmL^{-1} of Al, Cu and Fe impurities (in 0.1 and 1 M HCl for Ln and Ac resins respectively) were prepared. $\text{Cu}(\text{NO}_3)_2 \cdot 3\text{H}_2\text{O}$, $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ and $\text{Al}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$, were used as suitable salts.

3-The samples were prepared for each particular resin and repeated.

4-To reduce Fe^{+3} to Fe^{+2} , different amount of Vitamin C (ascorbic acid) was added to each sample.

5-The columns were preconditioned with 5mL HCl (0.1 and 1M for Ln and Ac resins respectively).

6-Sample solutions which were obtained using 1mL of mixed metal solutions (containing 1mg/mL of each one of traces) were evaporated to dryness then redissolved in 5 mL of appropriate acid concentrations.

7-The prepared samples above were loaded into the columns and were collected in the vials.

8-The columns were washed two times with 5 mL HCl (desired concentration for each resin). Then the effluents were collected into the two separate glasses vials (22mL volume).

9-The columns were washed with 5 mL HCl 6M. This stage was performed too see whether the metal impurities can be extracted in this condition.

10-All the above steps were repeated with adding different amounts of Ascorbic acid (VC) (0, 10, 100 and 500 mg).

11-The resulting solutions in each elution fraction were then allowed to settle and then were subjected to ICP-OES.

These results are explained in detail in chapter 4.

It was necessary to determine the metal trace contaminations in blank and background samples. The background and blank samples were prepared and were analysed by ICP-OES. The results are given in Table 3-3.

Table 3-3: shows the contents (ppm) of the trace metals in A0 and BG samples via ICP-OES

Sample name	Al167(a) ppm	Al 176(b) ppm	Ave(a &b) ppm	Fe ppm	Cu ppm
A ₀ 1	42.01	38.9	40.455	38.55	40.22
A ₀ 2	57	52.2	54.6	55	56.5
B(VC-500mg)	0.4699	0.3016	0.38575	0.1887	0.2802
B(VC-500mg)	0.1455	0.517	0.33125	0.1632	0.2547
B(VC-100mg)	0.963	0.013	0.488	0.2578	0.2936
B(VC-100mg)	0.599	0.2287	0.41385	0.1083	0.2094
B _H (HCl 1M)	0.894	0.0095	0.45175	0.2198	0.3002
B _H (HCl 1M)	0.0914	0.0092	0.0503	0.246	0.3055
B _p (NO ₃ H)	1.322	0.355	0.8385	0.3195	0.298

Where:

A₀ represents samples for ICP-OES analysis containing 1mg/mL of the metal trace solution prepared according to 3.3.8.1.1.

B samples are blank samples containing different amounts of Ascorbic acid (0, 10, 100 and 500 mg).

B_H samples are blank samples containing HCL 1M.

B_p is a blank sample containing HNO₃.

3.3.9 Final Indium recovery (extraction)

In order to measure the recovery of ¹¹¹In (R_{in} in % or percentage of standard) in our elution studies and our separation procedures, which are described in this chapter, an elution study was performed with a combination of high concentration inactive Cadmium and moderately high concentration of other metal impurities (Fe, Al and Cu) in the radioindium sample solutions.

In previous radioindium separation methods, elutions of ¹¹¹In are incomplete and the yield of ¹¹¹In obtained were about less than 70 % /san96/.

The samples loaded onto the columns were prepared with 100 µL of the standard solution of ¹¹¹In added in 5 mL increments of a mixed solution which contained 1 mgmL⁻¹ of metals impurities (Al, Fe, and Cu plus 100mg/mLof inactive Cd). The small Ln and Ac columns used were packed as described in 3.3.3. Sample preparation methodology for this experiment is explained in 3.3.9.1 below.

3.3.9.1 Sample preparation and procedure

1-The samples were prepared from 1mL metal solutions of (Al, Fe, and Cu) plus 1mL of inactive Cd of high concentration (100mgmL⁻¹) plus 100µL¹¹¹In (radioindium standard solution).

2-The prepared sample was evaporated and then redissolved in 5 mL HCl 0.1 M for doing experiments with Ln columns and redissolved in 5mL HCl 1 M for Ac columns.

3-100 mg Vitamin C was added to each sample.

4-The samples were loaded onto the columns.

5-The columns were washed two times with 5mL HCl (0.1 and 1 for Ln and Ac-columns respectively).

6-Then the columns were washed again with 10 mL HCl 6M. This fraction was collected into a 22mL glass vial.

7-Last steps (^{111}In fraction) were evaporated to dryness, then the residue redissolved in 5mL of appropriate HCl concentrations.

8-10 to 15 mL LS cocktail were added to the vials. The vials were counted using the LSC method.

The calculations of the recovery of the ^{111}In standard for Ln and Ac resins showed roughly 85% recovery (more details in chapter 4).

3.3.10 Simulated experiment

After comparing all data and conditions used in In/Cd separation, with Ln and Ac Resin, it was suggested that the use of a combination of Ln Resins® and Ac Resins® would be the best suited condition for this purpose. In a “Simulation experiment” Ln an Ac columns were used in tandem in an elution or separation experiment.

3.3.10.1 Sample preparation and procedures

The two separation steps started using Ac columns, and then the fraction from the washing step with 6 M (HCl) was loaded onto the Ln columns as sample loading. For the determination of the ^{111}In recovery, only the washing fractions with 6 M (HCl) from the Ln columns were counted.

The stages of this separation procedure are listed as below;

1-Three different Ac and Ln columns were prepared as described before in this chapter (3.3.3). 6 small columns were prepared.

2-5 mL of mixed solutions were prepared six times according to 3.3.9.

Since the separation procedure was started using Ac Resin®, the mixed solution of metal impurities and high concentration of inactive Cd, had to be prepared in HCl 1M.

3.3.10.1.1 Separation steps

1-The Ac columns were conditioned with 5mL HCl 1M.

2-5mL of mixed inactive solution containing 100 μ L ^{111}In was loaded onto the Ac columns.

3-The Ac columns were washed two times with 5mL HCl 1M.

4-The columns were washed with 5mL HCl 6M. These fractions were collected in glass vials as (A) samples (the ^{111}In fraction in this step).

5-(A) samples were evaporated and redissolved in 5 mL HCl 0.1 M to be used as sample loading on the Ln columns.

6- Ln columns were conditioned with 5 mL HCl 0.1 M.

7- The solution described as (A) samples were loaded on the Ln columns. Hence the last wash steps with Ac columns were used as sample loading on the Ln columns.

8-The columns were washed two times with 5mL HCl 0.1M.

9-Then the columns were washed with 5 mL HCl 6M. These fractions were collected as (B) samples (last ^{111}In separation fraction).

10-The (B) samples were evaporated to dryness then redissolved in 5mL HCl 0.1 M.

11-10 mL liquid scintillation cocktail were added to the samples. The samples were counted by LSC. The result will be explained at chapter 4.

This experiment has to be repeated with ^{109}Cd , in order to determine D_f factors in the fractions containing ^{111}In .

This schematic view of the presented fast and convenient chemical purification and separation procedure (^{111}In in presence of high amounts of Cadmium) is shown in Fig. 3-11. The individual steps have been explained in detail in 3.3.10.1.1.

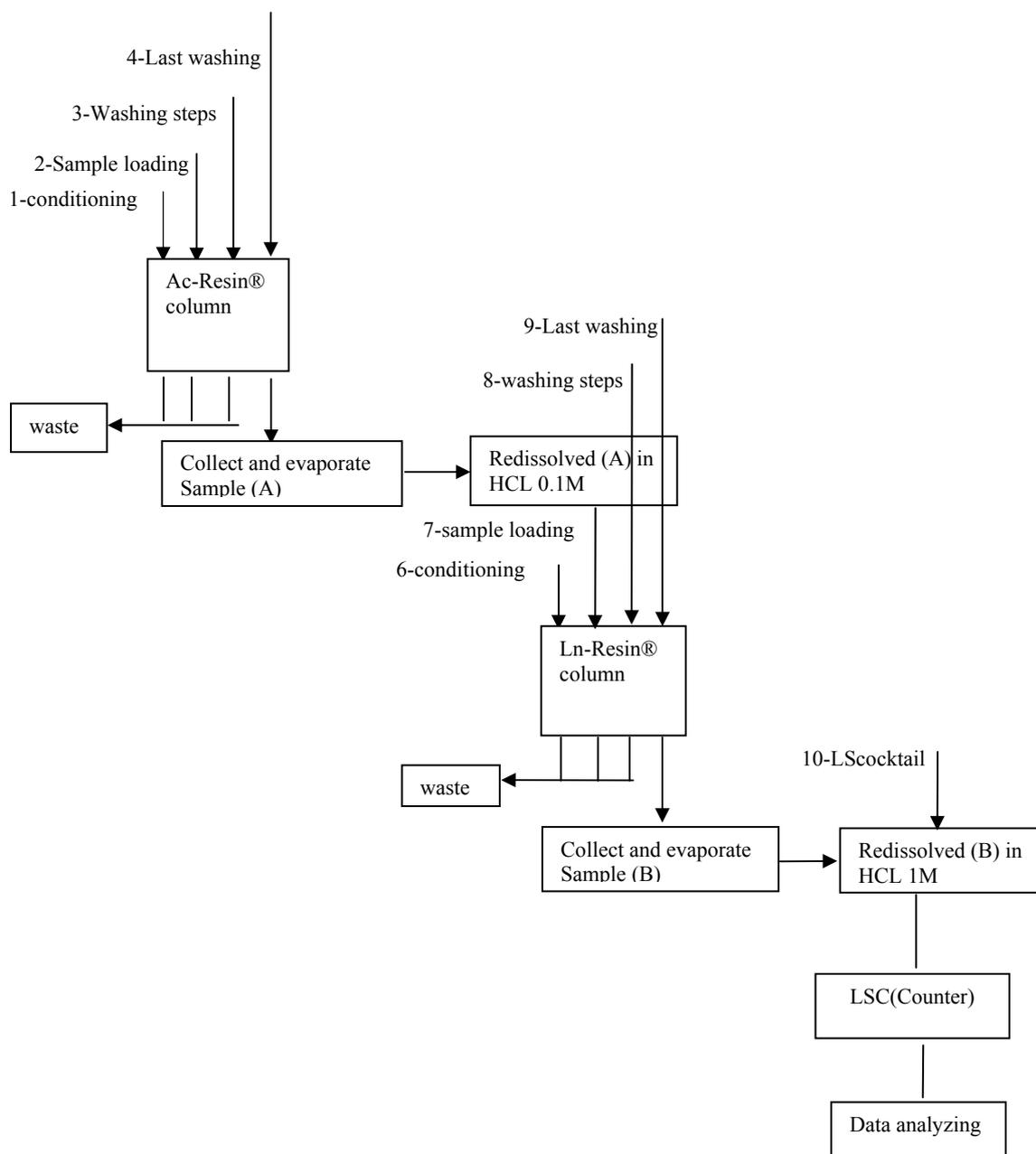


Fig 3-11: Schematic illustration of the simulated procedure for separation and chemical purification of ^{111}In from Cadmium.

3.4 ^{109}Cd Recovery

In order to find the conditions best suited for selective recovery of highly enriched ^{112}Cd from dissolved targets, several D_w value determinations and elution studies had to be performed. The procedures were the same as those for ^{111}In separations.

3.4.1 Evaluation of D_w values

D_w studies for ^{111}In and ^{109}Cd , with TEVA Resin® using different acids (HNO_3 , H_2SO_4) in different concentrations (from 0.001 to 6 M) have been done as well (3.3.1) to compare the results derived from measurements with the TEVA Resin® and different HCl concentrations. As we expected and will see later in chapter 4, D_w values are roughly the same and the difference between D_w values are not high enough to choose a condition for elution studies. It is found HCl is the most selective acid for separation when used with different SPE materials like TEVA, Ln, and Ac resins. Additional D_w experiments were performed with a very low HCl concentration at pH 5 and also with deionised water. All D_w experiments have been done using centrifuging method as described in 3.3.1.1 (b).

3.4.1.1 D_w values experiments (TEVA Resin® water and HCl pH5)

In this case we have to evaporate the ^{111}In and ^{109}Cd solutions to dryness and redissolve the residue in purified or deionised water and/or in HCl pH 5, to prepare the standard solutions. As we will discuss in chapter 4, the results are very suitable for $^{111}\text{In}/^{109}\text{Cd}$ separation with high differences in the D_w values. These D_w value determinations were done without preconditioning the weighted resin caps.

3.4.1.1.1 Sample preparation

1 mL of ^{109}Cd and/or ^{111}In standards (solutions in deionised water and/or in HCl pH 5), were pipetted into the Eppendorf caps containing 10 mg TEVA Resin®. Other separation steps were the same as those described in the centrifugation method 3.3.1.1 (b).

In this experiment the A_0 samples were prepared by taking 1 mL of the radioisotope standards. The advantage of this method (without preconditioning), was a decrease in the errors during sample preparation.

3.4.2 Elution study (TEVA prepacked columns)

Several elution studies were performed using prepacked TEVA columns with eluents:

a- 3 mol/L HCl

b- 9 mol/L HCl

c- deionised water (0 mol/L HCl)

The elution behaviour of Indium and Cadmium cations on the TEVA Resin® column was evaluated using procedures described in 3.3.2. Elution curves were obtained by washing aliquots of 5 mL of HCl of known concentrations (3M, 9M) and/or water, followed by determination of the activity of the eluate. The R_{In} (in %) and R_{Cd} (in %) values of the radioisotopes were calculated by equation (3).

In each experiment columns were preconditioned with 5 mL HCl at the desired concentration, and/or with 5 mL purified water. ^{111}In tracer and/or ^{109}Cd were loaded onto the column in small volumes. The elution steps were then started by adding aliquots of 5 mL of the appropriate acid and/or deionised water. The elution fractions were evaporated to dryness, and the residue redissolved in 5 mL HCl of a very low concentration and/or in deionised water. Then 5 mL of the LS cocktail (Highsafe) were added to the collected effluents and the samples were counted via LSC. The elution steps were continued until ^{111}In and/or ^{109}Cd were quantitatively removed from the columns.

The results show (see chapter 4) that, low concentrations HCl and/ or water could be the selective condition for Indium and/or Cadmium separation (recovery).

3.4.3 TEVA Resin®, ^{111}In extraction and ^{109}Cd recovery

In order to find a condition suitable for ^{111}In separation and ^{109}Cd recovery several elution studies were performed with TEVA prepacked columns and HCl 2M. In addition the influence of metal impurities and inactive Cadmium at high concentration were examined under these conditions.

3.4.3.1 Sample preparation (without adding any impurities)

1-the columns were Preconditioning with 5 mL HCl 2 M.

2-100 μ L ^{111}In and/or ^{109}Cd were added into 5mL HCl 2 M as sample solution. And then were loaded on the columns.

3-The columns were washed two times with 5 mL HCl 2M.

4-Then the stages above were continuing with washing the columns two times with water.

All the steps above were collected in the 22 mL volume glass vials.

5-To avoid chemical quenching, the collected effluent from (HCl 2M) were evaporated, and the dry residue were dissolved in 5 mL of HCl 0.1M or water.

6-10 mL SC (scintillation cocktail) were added to the samples, then the samples were cooled in the refrigerator.

7-The samples were counted for 10 min in Tri-Carb LSC or 5 min in Quantulus LSC.

100 μ L of the ^{111}In and/or ^{109}Cd radioisotope standard, were chosen as A_0 samples. Then the recovery R_{In} (in %) were calculated. The disintegration per minute (dpm) of the A_0 samples have to be more than 10000 (dpm).

The experiments were repeated three times. Cadmium remained on the columns even after washing with 10 mL water however Indium was eluted from the columns with 10 mL water. To remove all ^{109}Cd from the TEVA columns (Cadmium recovery), some parameters have to be changed, for example the amount of TEVA Resin® used in the columns, the concentration and amount of HCl or another suitable acid or the addition of complexation agents such as (EDTA). It was shown that it was possible to remove all ^{109}Cd from prepacked TEVA columns after the separation steps described above (3.4.3.1) using two times washing steps with a solution containing 0.1 mol/L EDTA (in 0.1 mol/L HCl) as eluent.

3.4.3.2 Influence of metal impurities and inactive Cd on TEVA Resin®

Several elution studies were performed to evaluate the influence of inactive metal traces and inactive Cd at high concentration on the separation steps with 2 M HCl using TEVA prepacked columns.

3.4.3.2.1 Sample preparation and procedures

1-The columns were preconditioned with 5 mL HCl 2 M.

2-100 μ L ^{111}In and/or ^{109}Cd plus 1mL of trace element solution (1mg/mL of Fe, Al and Cu mixed solution) and 1 mL of inactive Cd (100mg/mL) were taken into the glass vials. These mixed solutions were evaporated to dryness. Then the residue were redissolved in 5 mL HCl 2M as the sample loading.

3-The columns were washed two times with 5 mL HCl 2M.

4-The washing steps were continued with washing the columns with 5 mL water. (all the wash steps were collect in the glass vials).

5-To avoid chemical quenching, the collected effluent were evaporated and then the dry residue were dissolved in 5 mL of HCl 0.1 M.

6-10 mL SC (scintillation cocktail) was added to the samples.

7-In order to decrease photoluminescence effect and reduce the quenching effect, the samples cooled in a refrigerator for one hour.

8-the samples were counted for 10 min in Tri-Carb LSC or 5 min in Quantulus LSC.

100 μ L of the ^{111}In and/or ^{109}Cd radioisotope standard were chosen as A_0 samples. Then the recovery R_{In} (in %) were calculated. The disintegration per minute (dpm) of the A_0 samples have to be more than 10000 (dpm).

This experiment was repeated three times.

It seems that Indium and Cadmium are not well retain on the columns under these conditions. For In this is not be a problem, since we want to remove ^{111}In anyway, but Cadmium can be kept longer on the column to allow its separation from Indium. Therefore the elution studies were continued changing the amounts of impurities added using the same procedures as described above. All results will discuss in chapter 4.

3.4.3.2.2 Determination of metal impurities via Atomic Absorption

An elution study has been done as described above for the evaluation of the metal traces impurities (Fe, Al and Cu), in the separation steps (without adding radioisotopes).

The quantitative measurements, were achieved via “Atomic Absorption Spectrometry” (AAS) method, an important and very sensitive technique for trace element analysis. The experiments were carried out by the working group of Dr. Skinbach at the chemistry department of the University of Marburg.

In each case, two individual samples were examined.

3.4.3.3 Possibility to re use the TEVA column

To show whether the TEVA columns could be used more than once an elution study was performed with one TEVA Resin® as shown below:

After collecting the last fraction (with 10mL water and EDTA for ^{111}In separation and ^{109}Cd recovery respectively), the columns were rinsed again with 5 mL water and/or EDTA and then were conditioned with 5-10 mL deionised water. The columns were used for next In-separation and/or Cd recovery experiments, up to 10 times. The results are shown chapter 4. It will be shown that each TEVA column can be re used for several times.

3.5 Real target experiment

All the experiments above have been done as the optimisation studies on the separation conditions using inactive materials such as Fe, Cu, Al, Cd and small amounts of ^{111}In and ^{109}Cd . The best selective conditions were examined to validate the separation condition using a real irradiated cadmium target (an irradiated cadmium target via CV-28 cyclotron in the mode of proton induced) with high activity and gamma spectrometry at Jülich Research Center (JRC).

The separation conditions worked out at nuclear chemistry department of Phillips University of Marburg should be used to compare the results.

3.5.1 General description of CV-28 Cyclotron

The cyclotron model CV-28 is a compact, isochronous, multi purpose radiation source where protons, deuterons, $^3\text{He}^{++}$ and alpha particles can be accelerated with variable energy up to 24, 14, 36 and 28 MeV respectively. It is a versatile machine which can be used in research and development in many fields such as radioisotope production, excitation functions studies, nuclear reactions, materials science, and others. Although it has seven external beam lines available, only three are operational and are located inside the cyclotron vault. The nominal characteristics are shown in Table 3-4.

Table 3-4: Nominal characteristics of the cyclotron CV-28

Particle	Energy (MeV)	I_{ext} (μA)	I_{int} (μA)
H^+	2-24	40-60	200
$^2\text{H}^+$	4-14	55-100	300
$^3\text{He}^{++}$	6-36	5-50	135
He^{++}	8-28	6-40	90

3.5.1.1 Irradiation condition

For each bombardment (in this work by proton induced) the appropriate metallic foil, dia. 13mm, was supported at the end of the external beam pipe in a remotely removable target holder which provided a vacuum-tight seal. The targets were cooled by 25°C water, flowing on the back of target, while the front surface was exposed to the cyclotron vacuum. The target thickness was selected so as to

maximize yield of the desired ^{111}In and minimize unwanted reaction e.g. production of $^{114\text{m}}\text{In}$ /Mac74/ Nie69/, by Dr. B. Scholten at JFZ (JRC).

Since the excitation functions for (p, 2n) reaction on ^{112}Cd are known (table 6 chapter 1), the proton beam energy of 20 MeV was chosen in order to maximize the production of ^{111}In via the (p, 2n) reaction on ^{112}Cd .

3.5.2 Targetry

3.5.2.1 Target material

A natural Cadmium foil of 0.125 mm thickness (Good fellow, 99.999%), 100mm X100mm (Fa. ChemPur Feinchemikalien und Forschungsbedarf GmbH, Karlsruhe) has been used to prepare the cadmium targets.

3.5.2.2 Irradiation test

Irradiations for the production of ^{111}In were performed at the compact cyclotron CV-28 at the Research Centre Jülich.

A test irradiation of a 0.125 mm thick Cd-foil (Good fellow, 99.999%) with a diameter of 13 mm for 15 min with 1 μA of 20 MeV protons was performed to estimate the yield of ^{111}In production. The activity at the End Of Bombardment (EOB) was about 2MBq (50 μCi).

3.5.2.3 Irradiation for separation experiments

Irradiated were a stack of seven Cd-foils each of 0.125 mm thickness (Good fellow, 99.999%) and a diameter of 13 mm for 7 h 20 min with 3 μA of 20 MeV protons. At the front and the back was a Cu-foil of 0.025 mm thickness to monitor the beam current.

3.5.3 Preparation of real sample solution

The irradiated target (seven-Cd foils) was left to stand 4 days to decrease the ^{109}In ($t_{1/2}$ 4.2h) and ^{110}In ($t_{1/2}$ 4.9h). After this desirable cooling time a different part (of known amount) of activated foil was dissolved together with 136 mg inactive Cd in concentrated HCl. The solutions were evaporated to dryness and the CdCl_2 taken up in 20 ml of various moles of HCl (0.1, 1 and 2 M) for different separation experiments with Ln, Ac and TEVA columns (SPE-materials). For each experiment 5 mL of these solutions were used.

a) Solution 1

A part (19.2 mg) of an active foil was dissolved together with 136.1 (13 mm diameter) inactive Cadmium in concentrated HCl. The solution was evaporated to dryness and the CdCl_2 taken up in 20 mL of 1 M HCl. For separation experiments (1-4) with Ac Resin 5 mL of this solution was used each time.

b) Solution 2

Another part (42 mg) of activated Cadmium foil was dissolved together with 136.1 mg (13mm) inactive Cadmium in concentrated HCl. The solution was evaporated to dryness and the residue of CdCl_2 taken up in 20 mL of 0.1 M HCl. For separation experiment 5 and 6 with Ln Resin 5 mL of this solution was used each time.

c) Solution 3

The remaining 10 mL of solution 2 was evaporated to dryness and the residue was taken up in 10 mL conc. HCl. For separation experiment (7) 5mL of this solution was used.

3.5.4 Activity detection

Gamma ray spectrometry was done using a high purity germanium detector (HPGe) with a relative efficiency of 30 %. The measuring geometry was located at 50 cm and 10 cm.

The detector was connected to an AMETEK-ORTEC multichannel buffer (919) and the software "Gamma vision" (ORTEC) was used for data acquisition and spectrum analysis.

3.5.5 Separations

Each 5 ml part of the solution was measured on the HPGe detector at 50 cm distance before starting separation as A_0 (standard sample). Also each loading, washing and fraction portion and the column after separation were measured on the HPGe detector at 50 cm or 10 cm distance.

The columns were conditioned with 5 ml of HCL with the same molarities of HCl of the loading samples. Seven separations experiments were performed. For conditions and final results see chapter 4.

3.5.5.1 Separation procedure

The separation steps were classified as below;

1-The columns (Ln, Ac and TEVA) were conditioned with 5 ml of HCL with the same molarities of HCl of the loading samples (0.1, 1 and 2 M respectively).

2-5mL of radio active solutions (described in 2.2) was loaded on the columns. The effluents was collected on separated plastic vials (20 mL volume).

3-The Ln and Ac columns were washed 2 times (each with 5 mL HCl 0.1 and 1 M respectively). The washed solutions were collected separately.

4-The Ln and Ac columns were rinsed (from radioindium) with 1 and 2 mL HCl 6M (^{111}In fractions) up to 10 times. All fractions were collected on plastic vials separately.

5-All separation fractions were counted under the same condition with the HPGe detector.

6-For TEVA columns the column was washed with HCl 2M up to 5 times. All fractions were collected on the plastic vials separately. In this case the sample loading was 5mL of active solution in 5mL HCl 1M.

7-Another experiment was done with TEVA columns. In this case the column was conditioned with 5mL HCl 12.1 M and the sample loading was 5mL of an active solution in concentrated HCl. The column was washed with 1mL of concentrated HCl up to 13 times. The fraction steps were continued with washing the columns with 2mL HCl 2M up to 3 times, then the column was stripped with 5mL water.

All fractions were collected on plastic vials separately and then counted with HPGe under the same conditions.

4 Results and discussion

As described in chapter 3, the D_w values as a measure of the distribution behaviour of Indium and Cadmium on different solid phase extraction materials, were determined in different acids or acid/salt mixtures of varying concentrations, in order to evaluate the best suited conditions for separation and purification of carrier-free ^{111}In from irradiated Cadmium targets

4.1 D_w values, TEVA Resin®

The figures 4-(1-6) below show the D_w values for ^{111}In and/or ^{109}Cd on TEVA Resin®

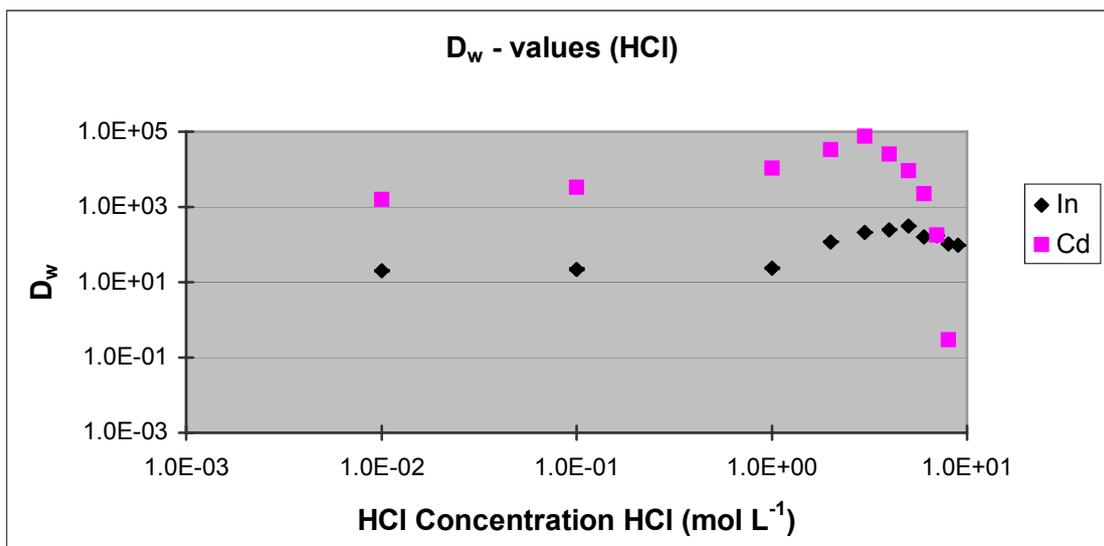


Fig 4-1: Weight distribution ratios (D_w) for In and Cd; different concentrations of HCl, on TEVA Resin®

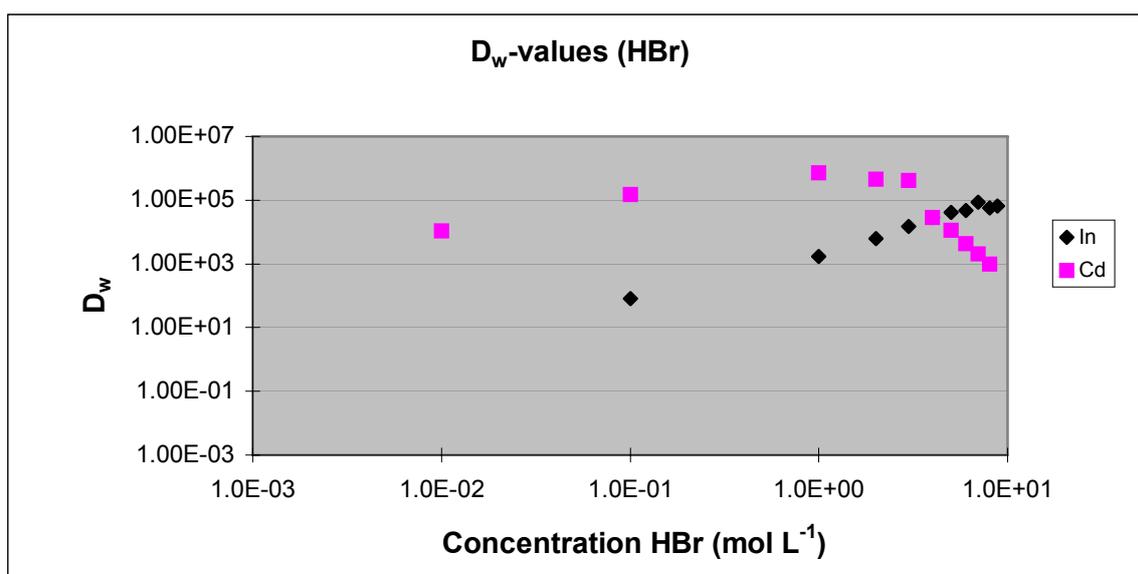


Figure 4-2: Weight distribution ratios (D_w) for In and Cd; different concentrations of HBr, on TEVA Resin®

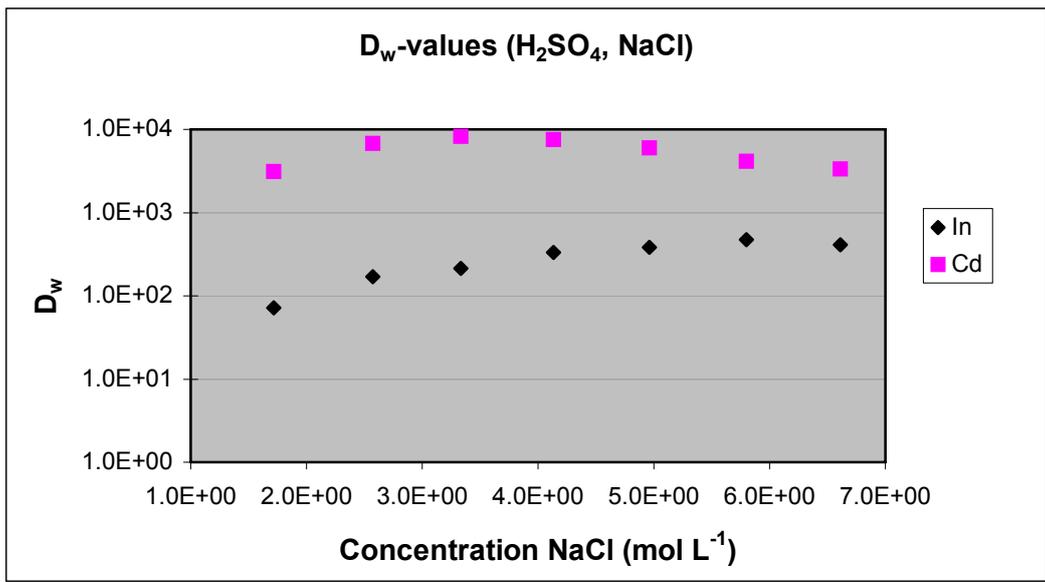


Fig 4-3: Weight distribution ratios (D_w) for In and Cd; 3 mol/L H_2SO_4 and different concentrations of NaCl on TEVA Resin®

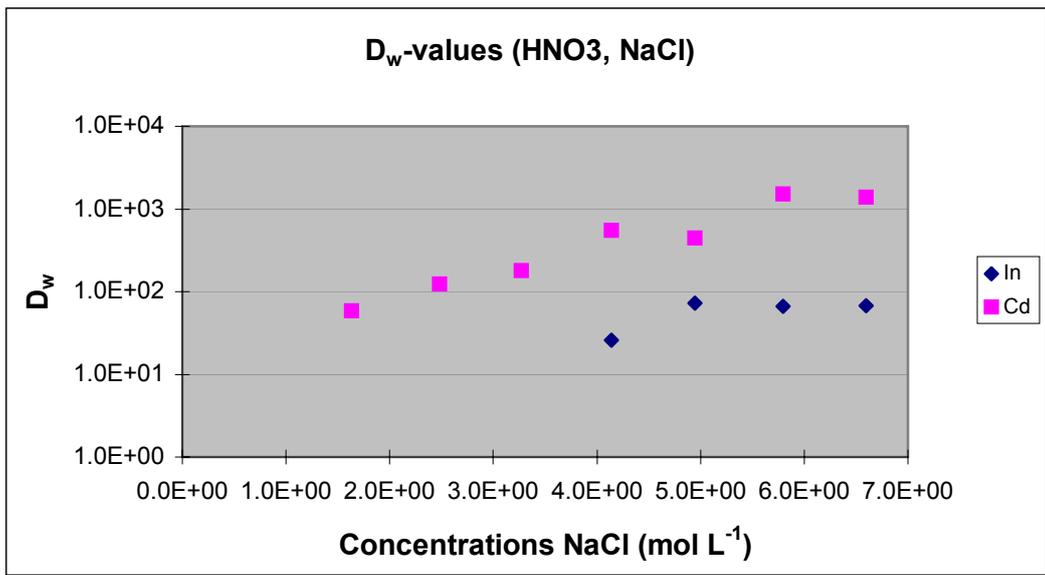


Fig 4-4: Weight distribution ratios (D_w) for In and Cd; 2 mol/L HNO_3 and different concentrations of NaCl on TEVA Resin®

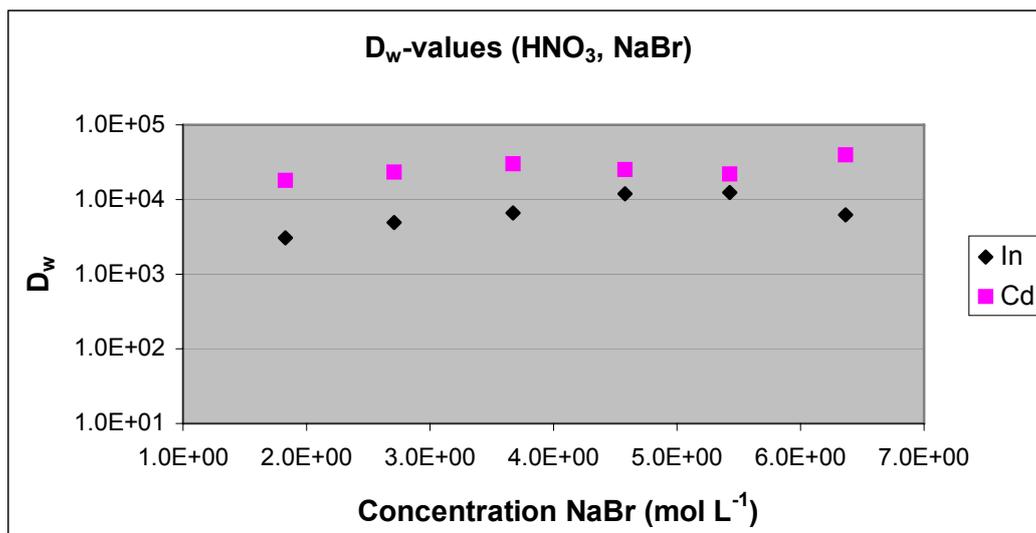


Fig 4-5: Weight distribution ratios (D_w) for In and Cd; 2 mol/L HNO_3 and different concentrations of NaBr on TEVA Resin®

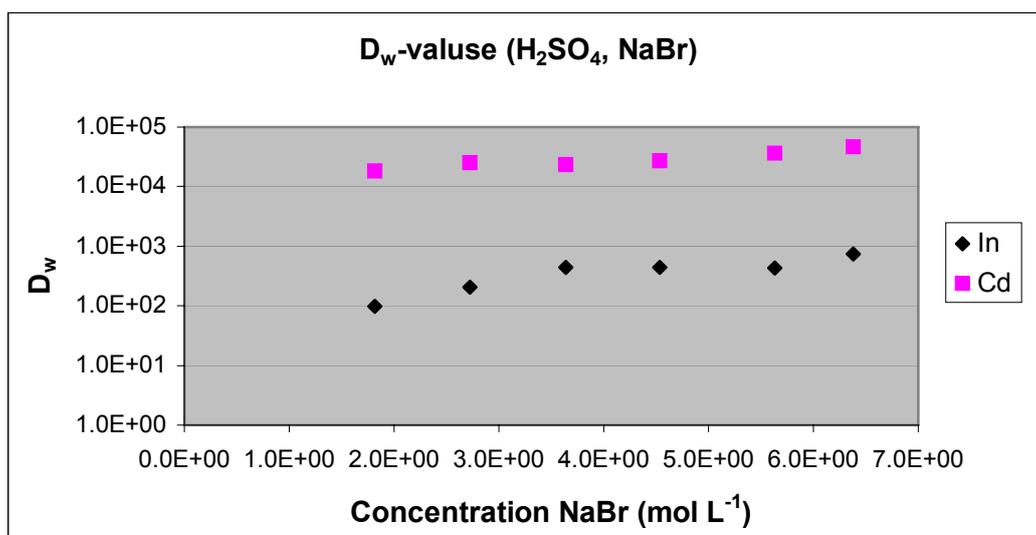


Fig 4-6: Weight distribution ratios (D_w) for In and Cd; 3 mol/L H_2SO_4 and different concentrations of NaBr on TEVA Resin®

As expected from literature /Raj94/Yam97/Zhe93/ Indium and Cadmium show very high distribution ratios in presence of high concentrations of chloride or bromide. According to the nature of the extractant used in the TEVA Resin®, namely Aliquat-336®, a soft Lewis acid, bromide complexes are extracted preferably since they are softer Lewis bases compared to the chloride complexes. Furthermore, the figures show that in general cadmium has higher distribution ratios than Indium. For both acids, HCl and HBr, the D_w values on TEVA Resin® show that an In/Cd separation

should be possible, However, taking into consideration the limited capacity of the disc, separation of Indium from macro amounts of Cadmium is very difficult, if not impossible, since both cations compete for the same free active sites.

4.1.1 Elution behavior of ^{111}In and ^{109}Cd on TEVA® Disc

A combination of TEVA extraction discs and HCl were considered to be well suited for removing Cadmium impurities, namely amounts that are well below the capacity of the disc, from purified ^{111}In solutions, as described in Chapter 3. Figures 4-7 - 4-9 compare the elution behaviour of Cadmium and Indium on TEVA Discs® HCl of varying concentrations was used for elution.

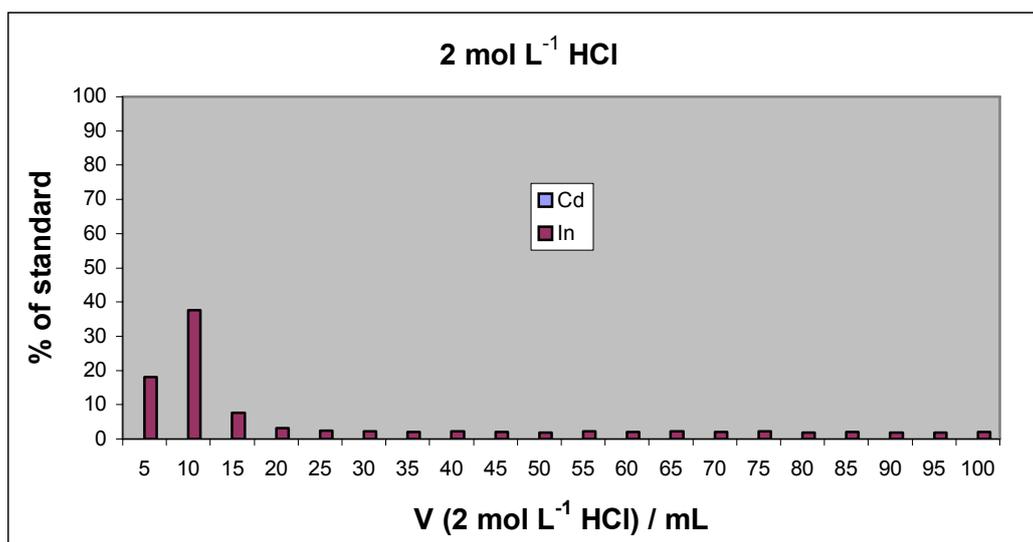


Fig 4-7: Elution profile 2 mol/L HCl

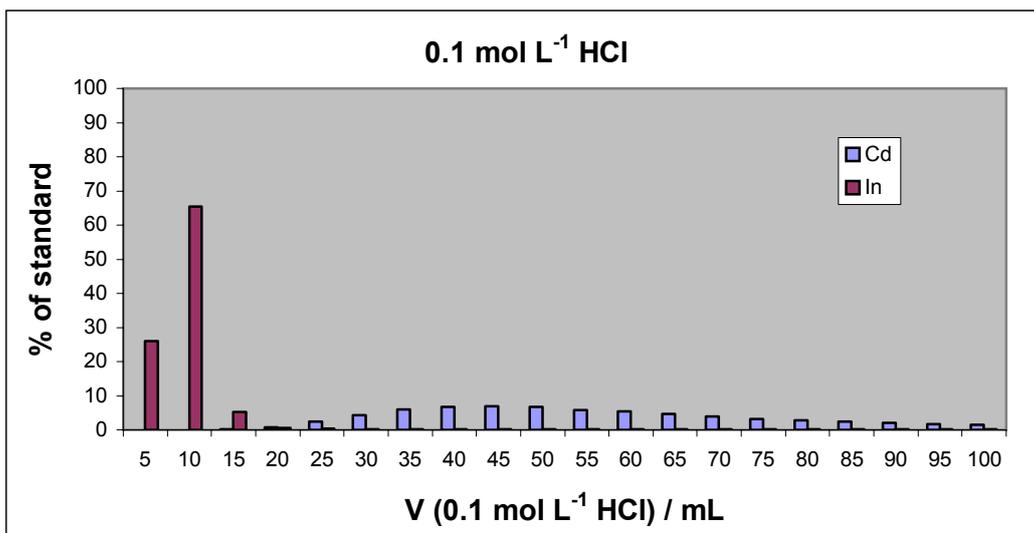


Fig 4-8: Elution Profile 0.1 mol/L HCl

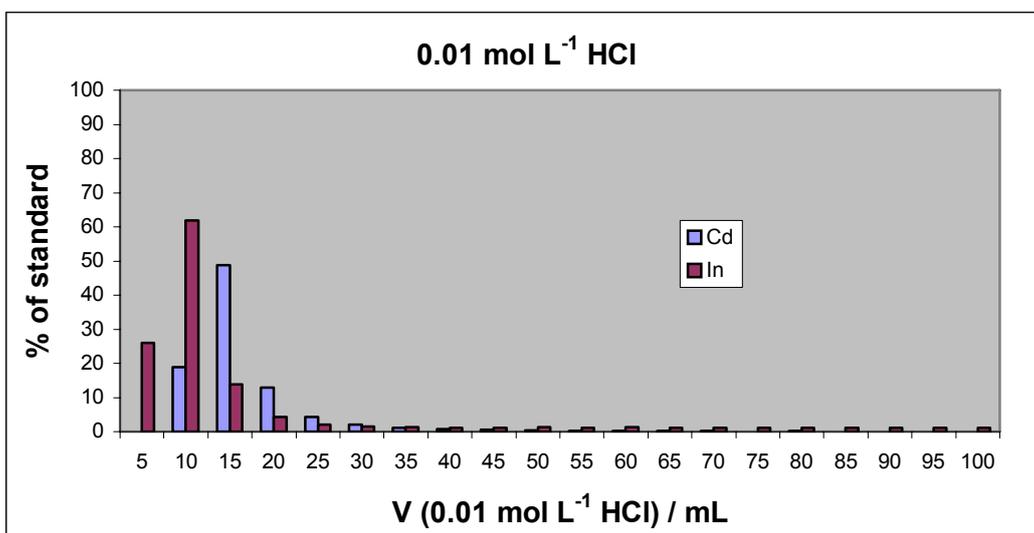


Fig 4-9: Elution profile 0.01 mol/L HCl

The above figures show that in any case Indium is removed when the discs are washed with 20-30 ml HCL. The elution behaviour of Cadmium is different, as was expected from the distribution ratios obtained using TEVA Resin. Figure 4-7 shows that no Cadmium is removed, even after washing with 100 mL of 2 mol L⁻¹ HCl. For 0.1 mol L⁻¹ HCl elution of Cadmium starts at a volume of 25 mL and continues until 100 mL and even further (figure 4-8). 50 mL of 0.01 mol L⁻¹ quantitatively removes Cadmium from the TEVA® Disc (figure 4-9).

All of the Cadmium and most of the Indium is extracted onto the disc at a HCl concentration of 2 mol.L⁻¹. By washing with 20 mL of 2 mol L⁻¹ HCl Indium is

removed while Cadmium stays on the disc. The described conditions can be used to remove trace amounts of Cd from purified ^{111}In solutions by adsorbing them on the disc, while letting ^{111}In pass.

4.1.1.1 Reuse of TEVA® Discs

The separation conditions described in chapter 4.1.1 were applied to ten ^{111}In and ten ^{109}Cd solutions of known activities using the same TEVA® Disc. Table 1, shows the recovery of ^{111}In standard and the decontamination factors (D_f) for ^{109}Cd standard. The mean recovery of the ^{111}In -standard was found to be 86,5 (+/- 9.2, k=1) %.

Table 4-1: ^{111}In -recovery in % and D_f of ^{109}Cd up to ten times from one TEVA® Disc with HCl 2 M

Number of experiments	recovery of ^{111}In standard R_{In} in %	DF of ^{109}Cd
1	68.7	10150
2	87.4	15450
3	95.7	6370
4	82.7	2070
5	93.4	2490
6	75.2	650
7	95.9	300
8	85.0	27
9	95.5	33
10	85.2	33

From the decontamination factor (D_f), the disc showed rather good performance for the first few applications. But as is indicated in Figure 10, performance decreased rapidly afterwards.

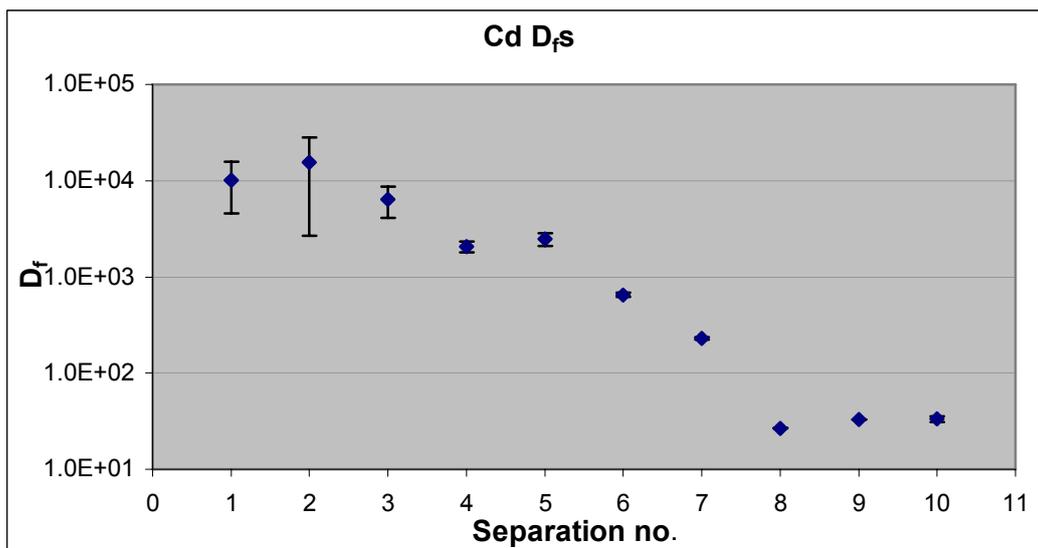


Fig 4-10: Cd decontamination factors; TEVA® Disc; repeated separations

From the Indium recoveries and Cadmium decontamination factors (table 4.1), it can be concluded that one TEVA® Disc might be used up to three times. The decontamination factors for Cd were found to be in the order of 10,000. As indicated by figure 4-9 a nearly quantitative Cd removal can be achieved by washing the disc with rather large amounts of dilute hydrochloric acid. Unfortunately the TEVA discs® showed lack of long term stability as indicated by the decrease in Cadmium D_f values. It was found that the disc should be replaced once used in three separations.

4.1.2 EDTA D_w values

It was investigated whether EDTA solutions are appropriate to aid in Cadmium removal from the disc, and it was found that aqueous solutions containing rather large amounts of EDTA (0.5 mol L^{-1} as well as 0.1 mol L^{-1}) solutions with hydrochloric acid concentrations greater than 0.1 mol L^{-1} , give low weight distribution ratios (D_w —chapter 4, Figures 11 and 12) and might therefore be used to remove Cadmium from the TEVA® Disc.

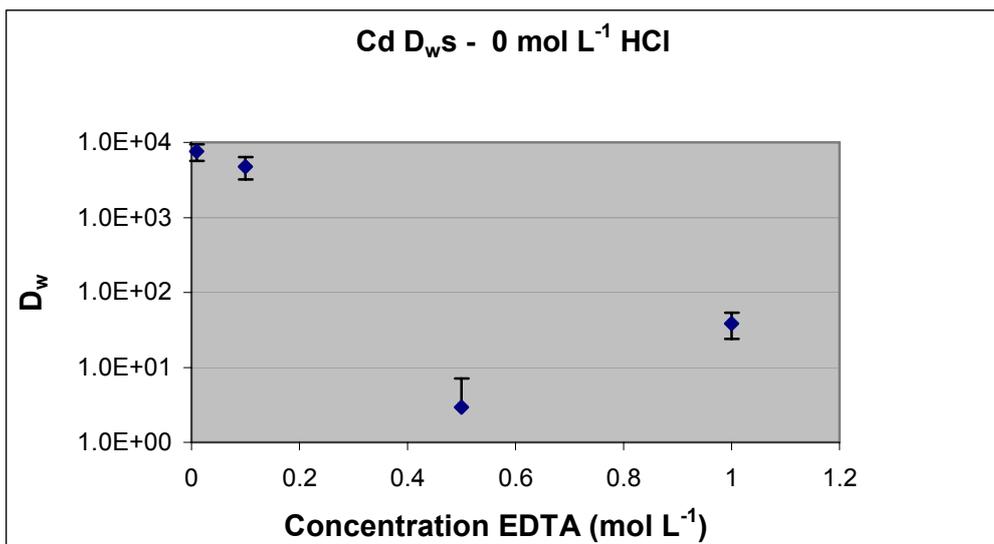


Fig 4-11: Cd D_w aqueous solutions of EDTA; TEVA® Disc

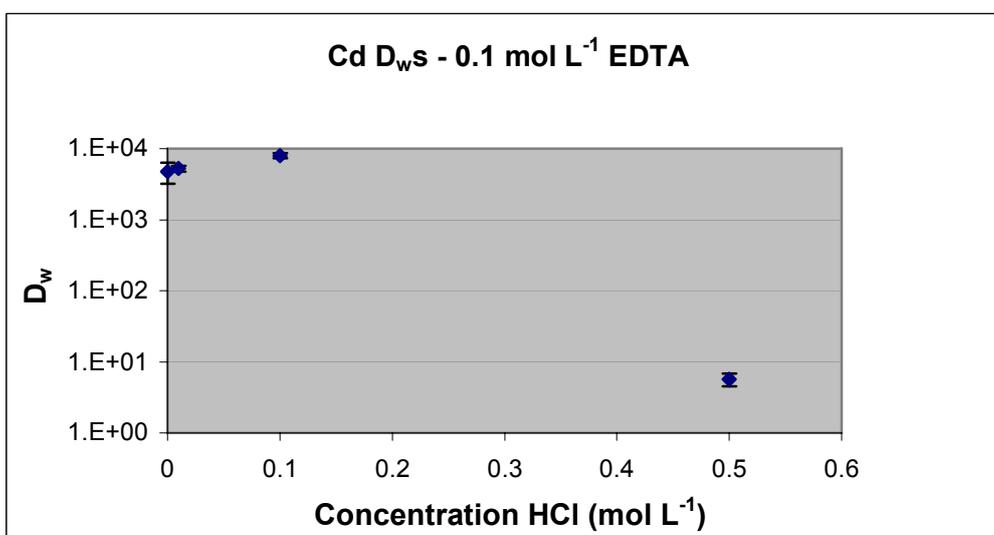


Fig 4-12: Cd D_w 0.1 mol/L EDTA solutions; varying HCl concentrations; TEVA® Disc

4.2 D_w values Ac Resin®, Ln Resin® and TRU Resin®

D_w curves for Ln, Ac and TRU resins; i.e., extraction chromatographic materials based on organophosphorus chelating agents for ¹¹¹In/¹⁰⁹Cd separation, were obtained for different concentrations of HNO₃ and HCl. The corresponding values are shown in chapter 4, Figures 13-18. The best experimental results were obtained

employing Ln Resin® and Actinide Resin®. Both resins were found to be well suited to separate ^{111}In from irradiated Cadmium targets. Conditions were established under which the difference in the D_w values of Indium and Cadmium were in the three or four orders of magnitude, with Indium D_w values being superior, meaning that the resins show higher selectivity for Indium. Nevertheless, there were also conditions that would allow Indium elution. HCl and HNO_3 were both found to be suitable media for the desired separation. However for further experiments, HCl was chosen with respect to the fact that HNO_3 is not considered an acceptable media for labelling reactions or medical application. This would necessitate an additional step to convert the obtained ^{111}In solution from nitrate to chloride media.

4.2.1 Ln Resin®, HNO_3 and HCl

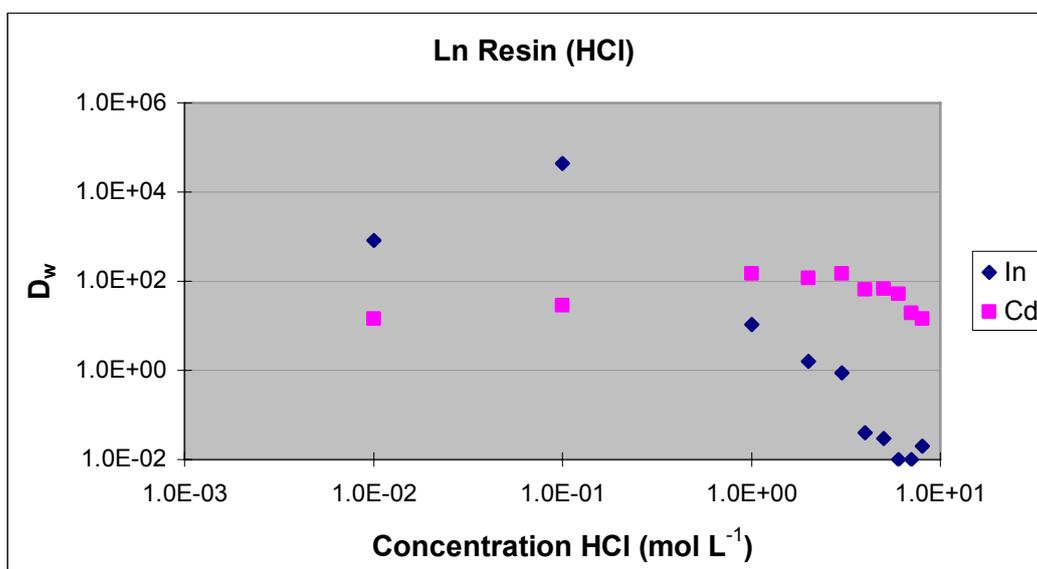


Fig 4-13: Weight distribution ratios (D_w) for In and Cd; different concentrations of HCl, and Ln Resin®

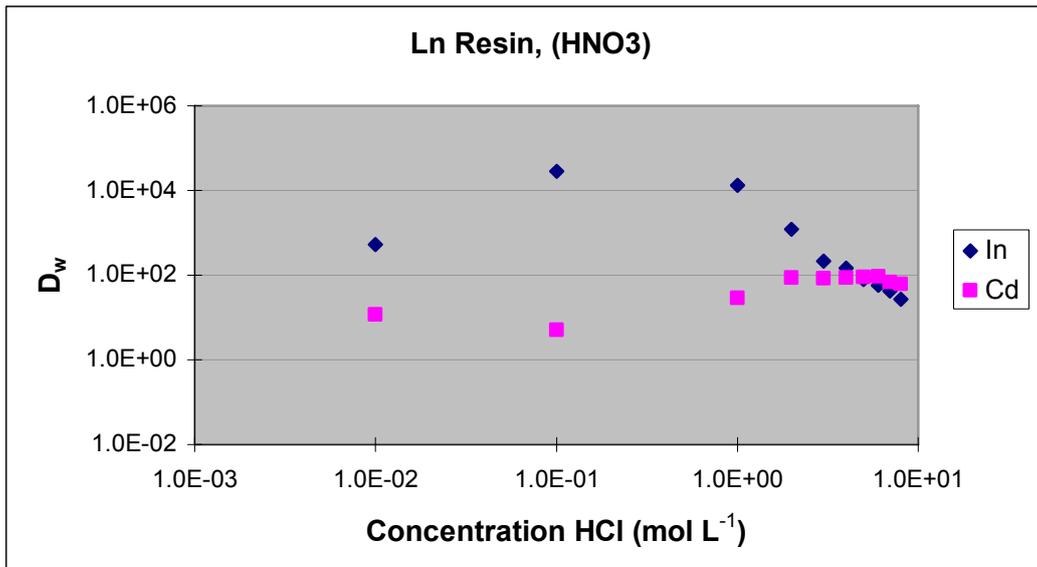


Fig 4-14: Weight distribution ratios (D_w) for In and Cd; different concentrations of HNO_3 , and Ln Resin®.

As can be seen in Fig 4-13, a combination of 0.1M HCl and Ln Resin® can be used for the separation of Indium and Cadmium, since both nuclides show a high difference in their corresponding D_w values. The extracted and purified Indium can then be eluted using HCl of elevated concentration (e.g. 6 M HCl). Fig. 4-14 shows that an $^{111}\text{In}/^{109}\text{Cd}$ separation is possible over a wide range of HNO_3 concentrations. The elution of In using HNO_3 , on the other hand, will be difficult.

4.2.2 Ac Resin® HCl, HNO₃

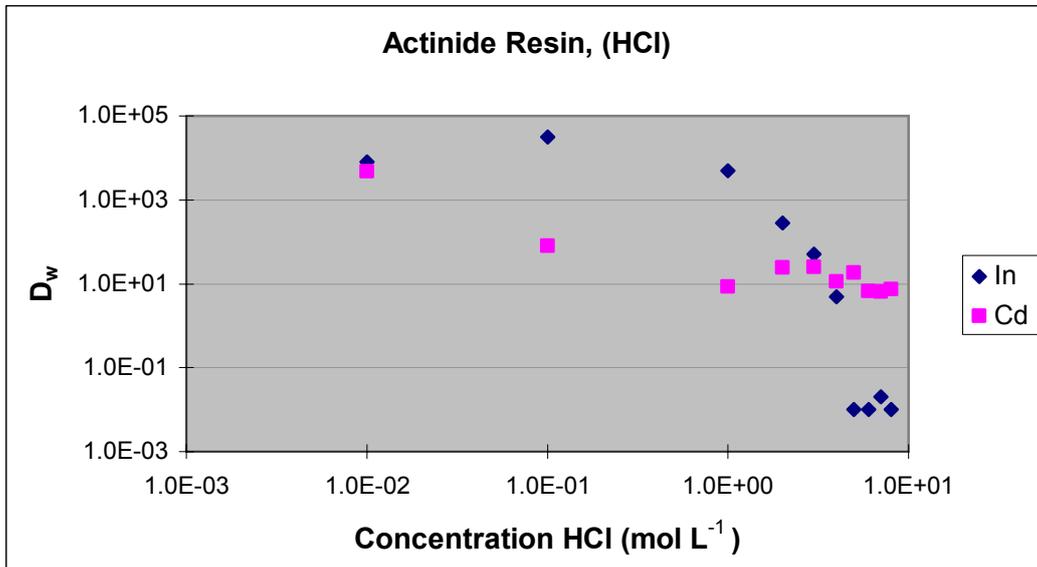


Fig 4-15: Weight distribution ratios (D_w) for In and Cd; different concentrations of HCl, and Ac Resin®

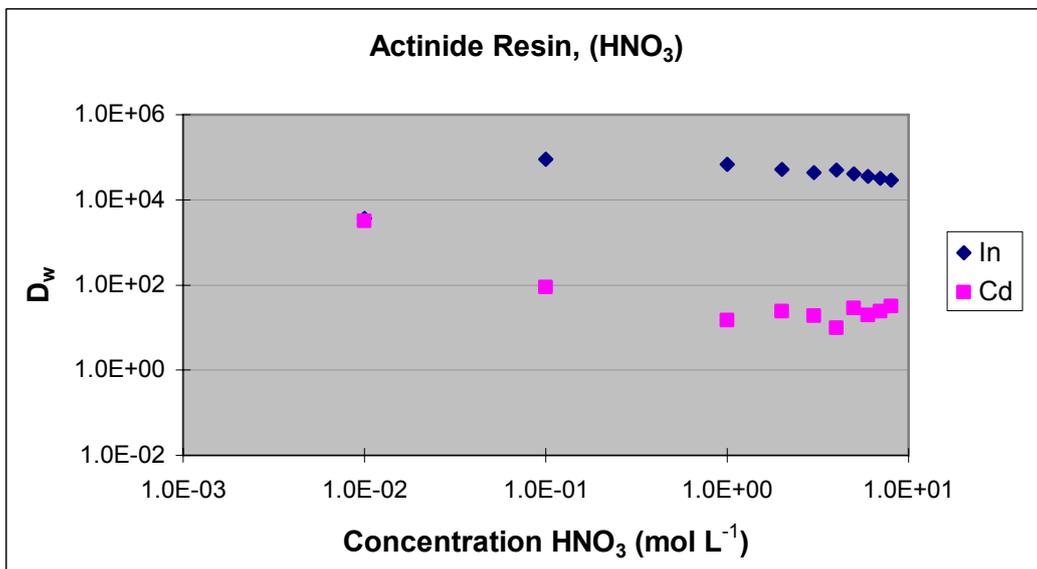


Fig 4-16: Weight distribution ratios (D_w) for ¹¹¹In and ¹⁰⁹Cd; different concentrations of HNO₃, and Ac Resin®

Figures 4-15 and 4-16 show that on the Ac Resin® an In/Cd separation is possible for HCl concentrations between 0.1 and 1 M and, as well as for HNO₃ concentrations \geq 0.1 M. Whereas for the Ln resin, an Indium elution is only possible under high HCl concentrations.

4.2.3 TRU Resin® HCl, HNO₃

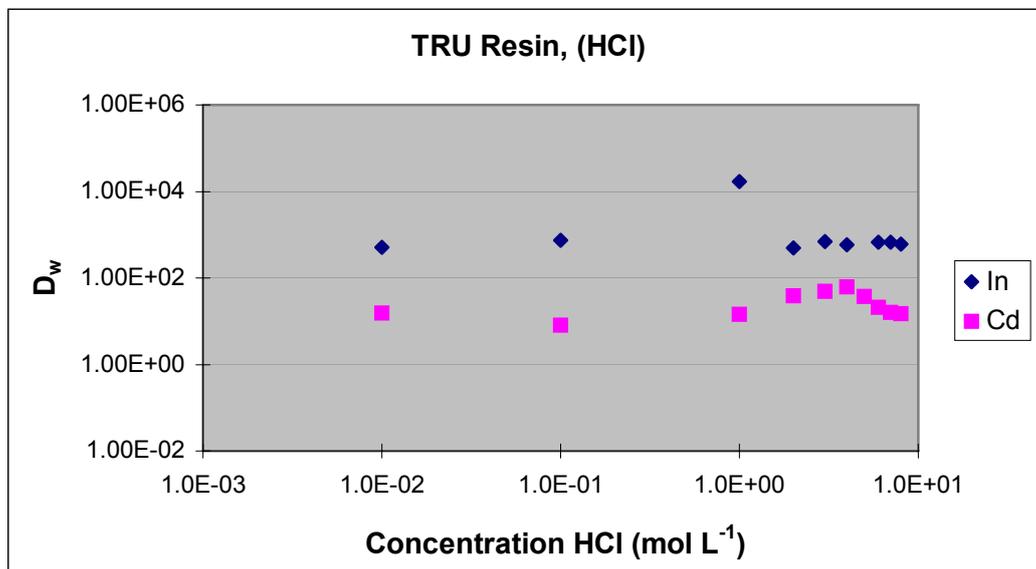


Fig 4-17: Weight distribution ratios (D_w) for In and Cd; different concentrations of HCl, and TRU Resin®

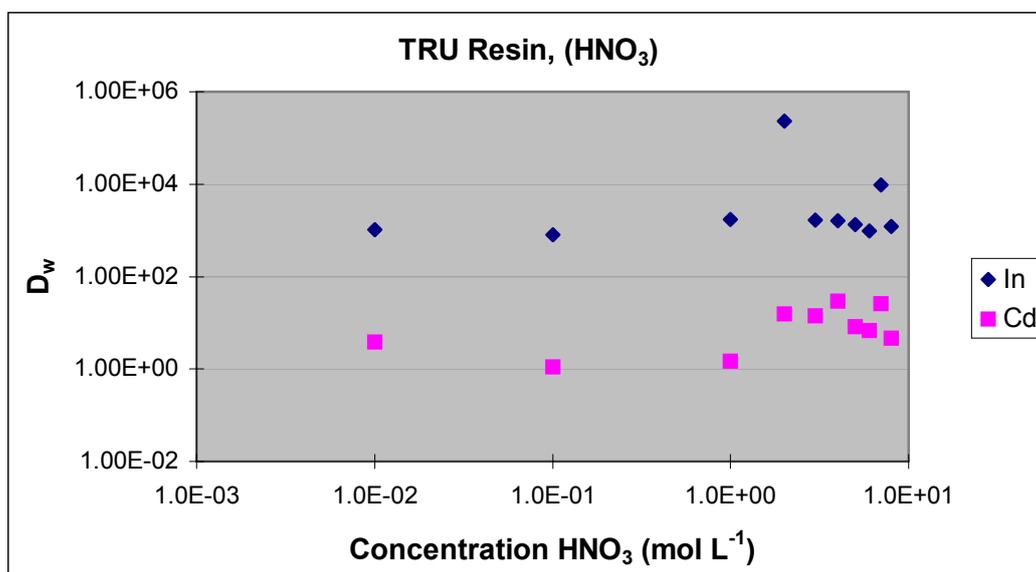


Fig 4-18: Weight distribution ratios (D_w) for In and Cd; different concentrations of HNO₃, and TRU Resin®.

Figures 4-17 and 4-18 show the D_w values obtained using the TRU Resin. Nor for HCl, neither for HNO₃ conditions allowing Indium/Cadmium separation and subsequent Indium elution.

4.3 Elution behavior of ^{111}In and ^{109}Cd on Ln and Ac resins

For Ln Resin as well as Ac Resin elution studies were performed in order to find rinsing and elution volumes, which allow high Cadmium decontamination combined with high Indium recovery. Figures 4-(19-22) show the results of the elution studies performed with Ln Resin® and Ac Resin® using different concentrations of HCl. Figures 4-19 and 4-21 show, that on the Ln Resin®, for 0.1 mol L^{-1} HCl no In-breakthrough is observed even after 100 mL, whereas Cadmium is readily eluted within the first 5 mL. On the other hand ^{111}In is quantitatively removed using 10 mL of 6 mol L^{-1} HCl.

Figures 4-20 and 4-22 show, that in the case of the Ac Resin®, no In-breakthrough is observed even after 100 mL of HCl 1 M, whereas Cd is readily eluted with 2.5 mL HCl 1M. On the other hand ^{111}In is quantitatively removed using 10 mL of 6 mol L^{-1} .

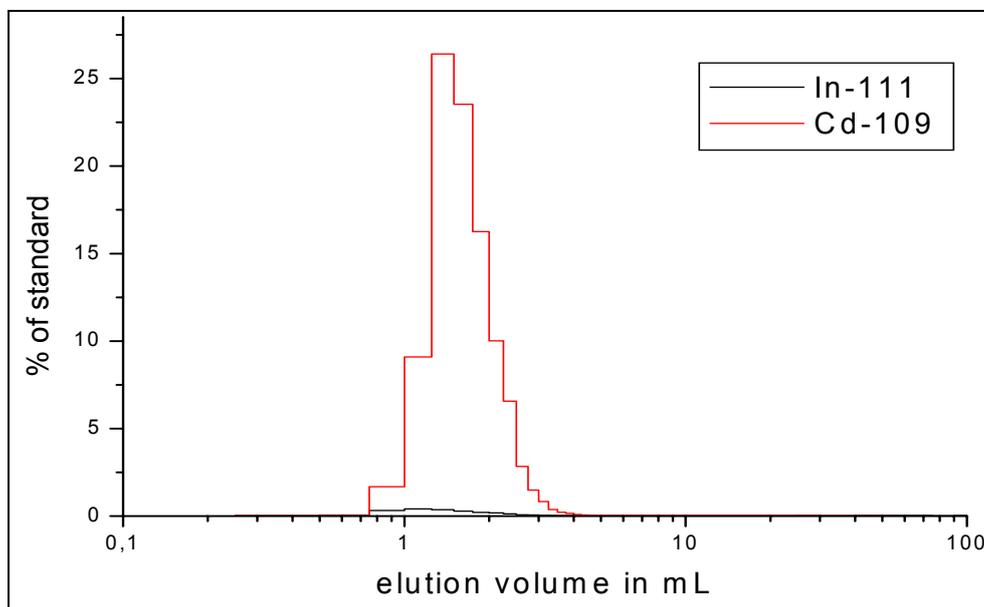


Fig 4-19: Elution study for ^{111}In and ^{109}Cd with HCl 0.1 M on Ln-resin®

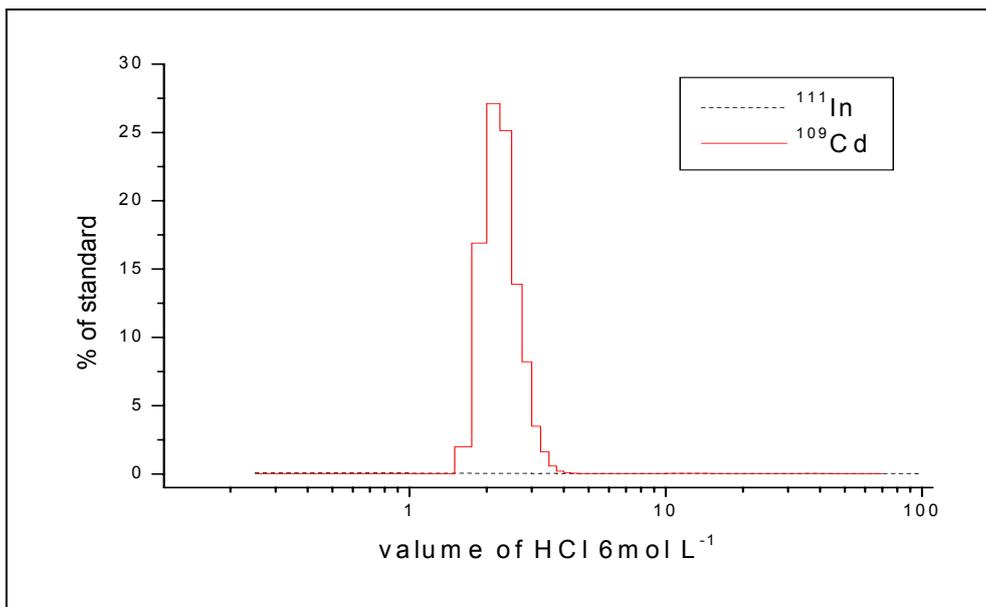


Fig 4-20: Elution study for ^{111}In and ^{109}Cd with HCl 1M on Ac-resin®

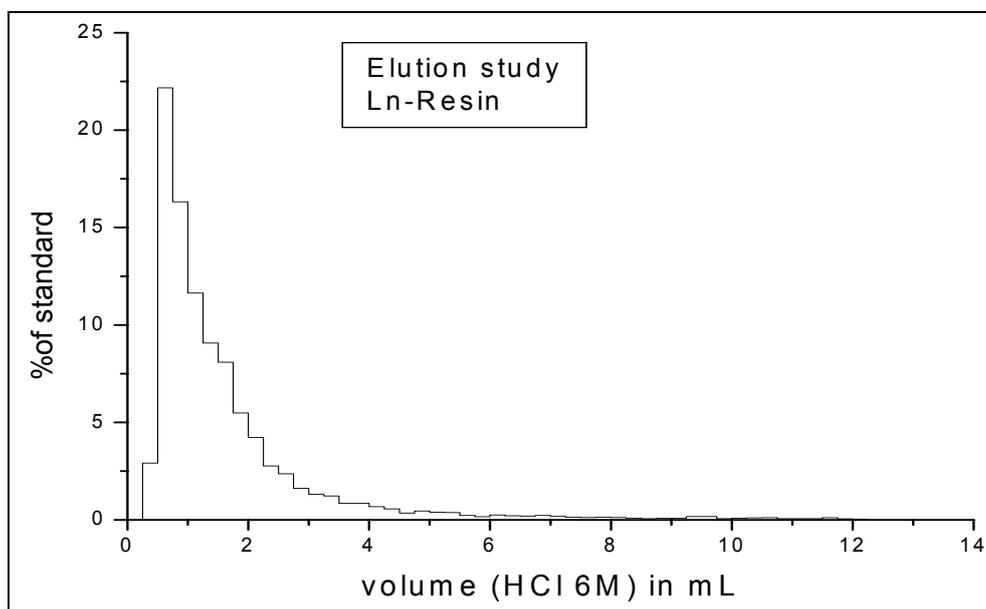


Fig 4-21: Elution study for ^{111}In on Ln Resin® with HCl 6 M

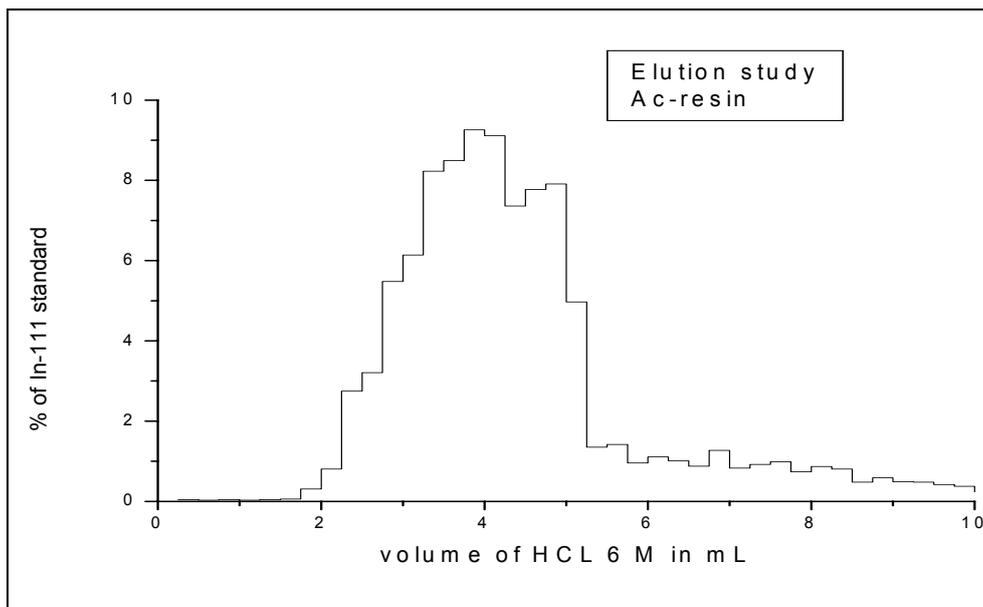


Fig 4-22: Elution study for ^{111}In on Ac Resin® with HCl 6 M

The diagrams 4-21 and 4-22 show that in any case (Ln Resin® as well as Ac Resin®), ^{111}In is removed effectively from the columns using less than 10 mL HCl 6M.

4.4 Influence of stable Cd, Fe, Al and Cu

One of the production methods for ^{111}In is the irradiation of natural Cadmium or enriched ^{112}Cd by proton and or deuteron beams in a cyclotron (see Chapter 1). In view of medical usage of radionuclides after bombardment, the produced ^{111}In must be separated from the Cadmium targets and other unwanted elements such as Cu, Fe or Al. These impurities may be found in the target material and/or target holder. Cadmium as well as potential impurities can be separated in a one-step procedure using the SPE technique. This work examined the impact of macro amounts of the mentioned cations on the Indium/Cadmium separation and on the Indium recovery as well as the chemical purity of the Indium fraction.

4.4.1 Influence of macro amounts of stable Cd on ^{111}In recovery

4.4.1.1 In D_w values

For the Ln Resin as well as for the Ac Resin, the influence of macro amounts of Cadmium on the ^{111}In D_w values was evaluated (see figures 4-23 and 4-24). For Ln Resin the influence is rather strong, nevertheless even in presence of 50 mg of Cd^{2+} D_w values in the order of 10000 were found. The Ac resin shows only very little interference by the stable Cadmium, the D_w values were roughly constant in the order of 4000 up to 90 mg of Cd^{2+} .

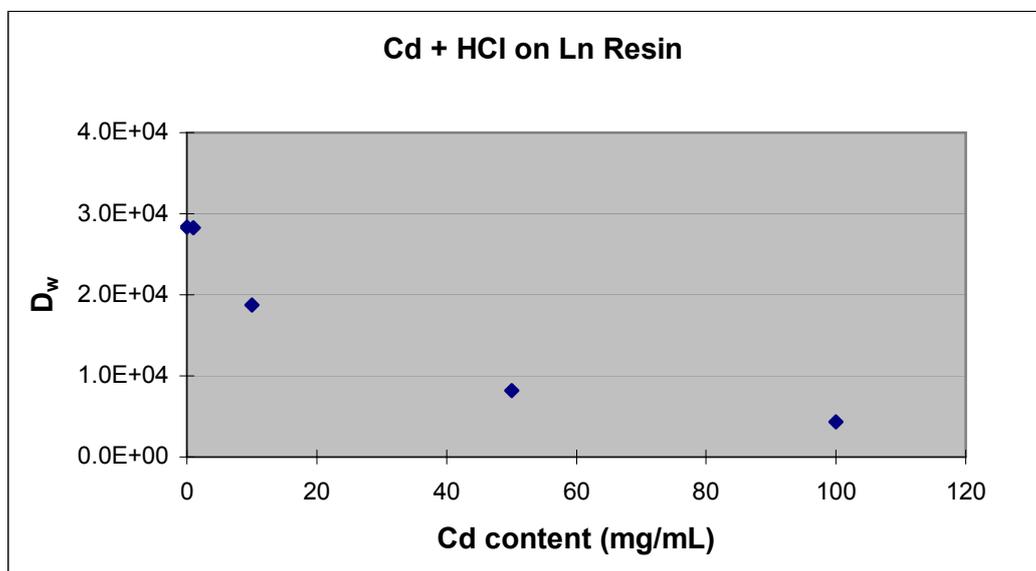


Fig 4-23: D_w values for Indium at macroscopic amounts of Cadmium

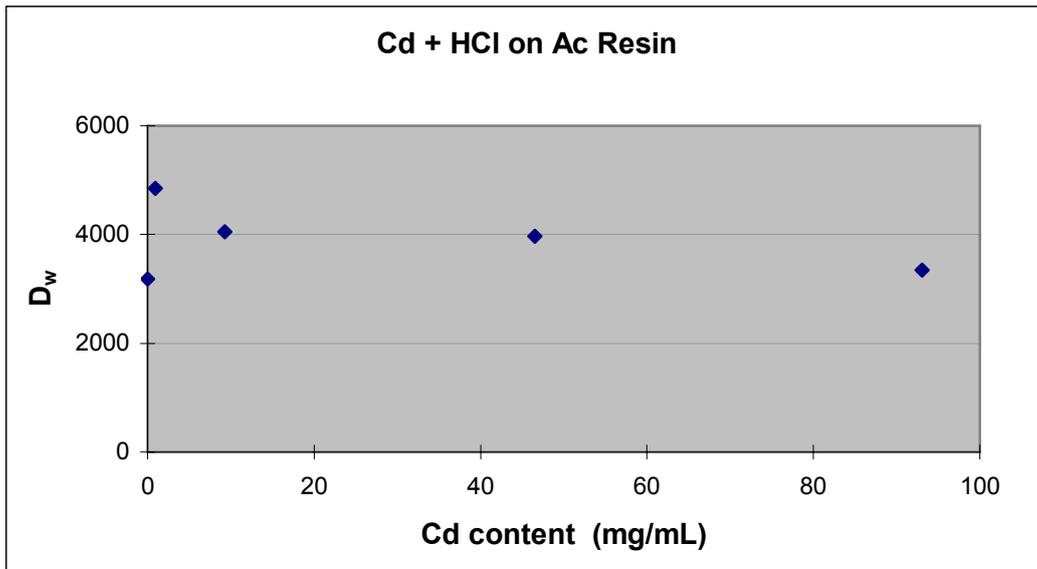


Fig 4-24: D_w values for Indium at macroscopic amounts of Cadmium

4.4.1.2 Elution study (In recovery and decontamination factors)

As expected the elution profile on Ln and Ac-Resins shows that a macro amount of stable Cadmium (up to 100mg), which was added to appropriately prepare ¹¹¹In standard solutions, has no influence on the ¹¹¹In recovery. The ¹¹¹In recoveries obtained for different concentrations of stable Cadmium are listed in tables 4-2 and 4-3.

Table 4-2: ¹¹¹In recovery with different amounts of stable cadmium, Ln Resin

m(Cd ²⁺) added / mg	¹¹¹ In recovery /%
0	101.0
1	101.9
10	100.8
50	100.2
100	102.0

Table 4-3: ¹¹¹In recovery with different amounts of stable Cadmium, Ac Resin

m(Cd ²⁺) added / mg	¹¹¹ In recovery /%
0	103.8
1	98.7
10	99.7
50	99.8
100	101.8

Results show that ^{111}In recovery under these conditions is close to 100%. In addition the D_f for Cadmium on Ln Resin® and Ac Resin® under these condition were determined. As it can be seen in table 4, the D_f values are greater than 20000. The separation thus provides a high enough Cadmium decontamination of the Indium fraction.

Table 4-4: Decontamination factors of Cadmium in ^{111}In stripping steps (breakthrough) Ac column

m(Cd2+) added/ mg	D_f
0	8458
1	23675
10	12542
50	23589
100	>30000

Table 4-5: Decontamination factors of Cadmium in ^{111}In stripping steps (breakthrough) Ln column

m(Cd2+) added/ mg	D_f
0	9215
1	9207
10	6407
50	19107
100	>30000

When the sample solution contained only Cadmium (e.g. from the target matrix) and irradiation products, the yield of the ^{111}In extraction was 100% as illustrated in Tables 4- 1, 4-2 and 4-3. ^{111}In is separated efficiently and quantitatively from a pure Cadmium matrix by Ln and/or Ac resins® when the total volume of rinsing was 5mL of HCl 6M.

The results shown in Tables 2-5 are summed up a comparative study shown in Table 6 which shows the separation conditions for the uptake of ^{111}In and ^{109}Cd by Ac Resin as a neutral exchange and by Ln Resin as an anion exchange. In any case using Ln and/or Ac columns as SPE materials, Cadmium will be easily removed from the columns within 5 mL wash with HCl 0.1 or 1 M, while ^{111}In under these conditions

strongly remains on the said columns. Then the ^{111}In can be easily removed from the columns with a total rinse of 5 to 10 mL HCl 6M.

Table 4-6: A comparative study for the Elution behaviour of ^{111}In and ^{109}Cd in different concentrations of HCl on Ln and/ Ac columns

Eluent	Volume of eluent mL	Amount eluted (%)		Resin
		^{111}In	^{109}Cd	
0.1 M HCl	5 mL	0	100	Ln-column®
6 M HCl	10	100	---	Ln-column®
1 M HCl	5 mL	0	100	Ac-column®
6 M HCl	10	100	---	Ac-column®

Table 4-6 shows that in presence of bulk amount of inactive Cd, selected conditions are very convenient for Indium/Cadmium separation when using Ln and Ac resins. In addition SPE method is one of the best selected methods, because it is fast and simple to perform and gives pure chemical fractions.

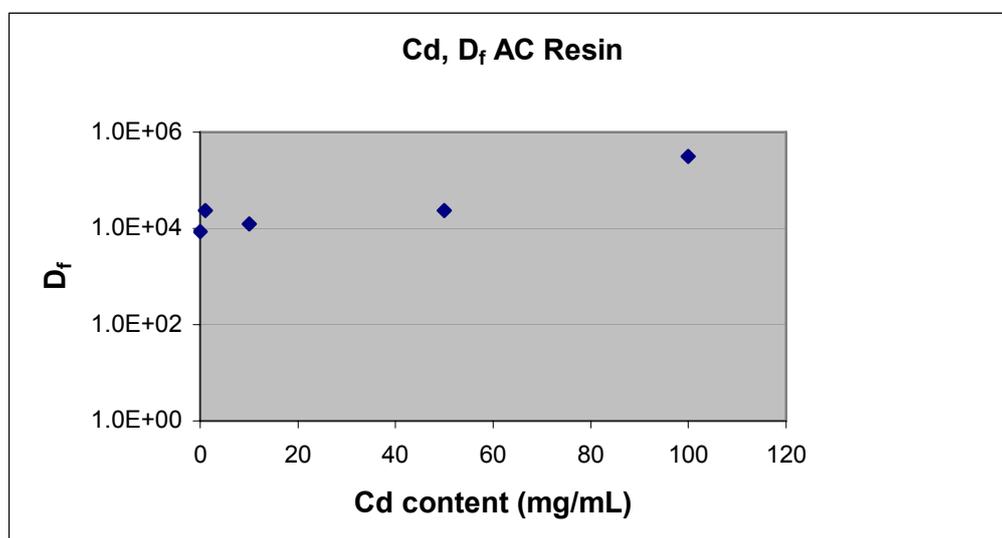


Fig 4-25: Cd D_f for different inactive Cd concentration with Ac column

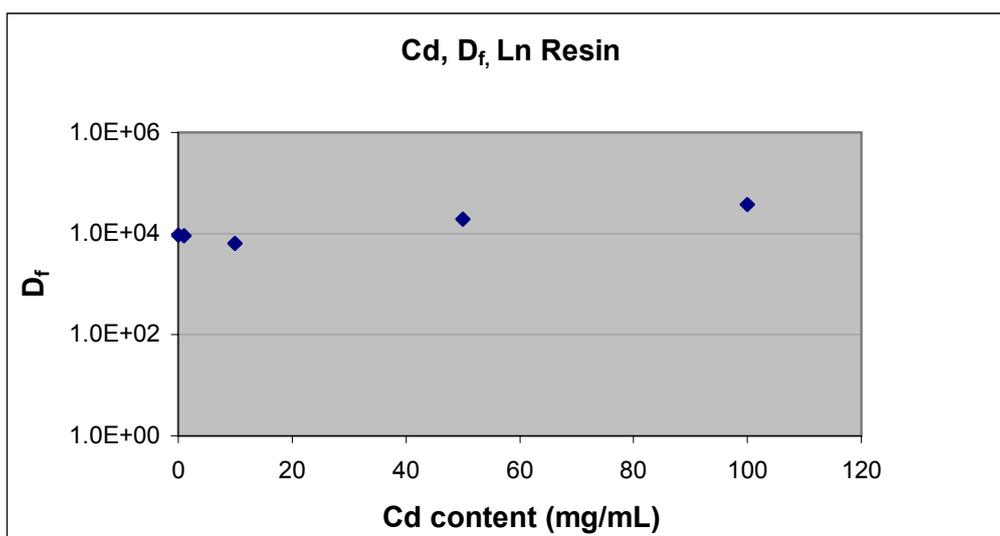


Fig 4-26: Cd D_f for different inactive Cd concentrations with Ln column

The Cadmium decontamination factors (D_f) were greater than 20.000 (at presence the inactive Cadmium concentrations up to 100 mg/mL) (see fig 4-25 and 4-26). It means this condition is very good for ¹¹¹In separation, hence the separation provided an excellent Cadmium decontamination in Indium fraction.

4.4.1.3 Reuse of Ln and/or Ac Resin

Ln and Ac Resins can be reused up to 8 times even when used for Indium separation in presence of high amounts of stable Cadmium. Tables 4-7 and 4-8 show the results of these separations.

Table 4-7: Reuse of Ln- Resin columns; ¹¹¹In recovery (in %); 8 repeated Indium separation; varying Cd contents

m(Cd ²⁺) added / mg	N° of replicated utilizations							
	1	2	3	4	5	6	7	8
0	100.0	99.5	100.6	109.2	97.2	102.9	102.1	108.0
1	100.9	101.7	107.6	108.3	100.6	102.1	92.3	100.7
10	99.2	100.6	100.2	107.6	102.0	101.9	102.1	98.8
50	99.8	100.4	100.1	101.7	100.7	101.2	102.1	95.0
100	99.1	100.5	100.7	105.2	99.8	109.1	103.2	98.1

Table 4-8: Reuse of Ac Resin columns; ^{111}In recovery (in %); 8 repeated Indium separation; varying Cd contents

m(Cd ²⁺) added / mg	N° of replicated utilizations							
	1	2	3	4	5	6	7	8
0	105.8	103.0	102.7	101.3	103.2	103.1	102.7	101.7
1	95.1	97.8	99.2	94.9	97.5	99.4	98.3	99.6
10	95.9	98.8	100.0	98.2	101.6	100.7	101.9	100.6
50	89.7	100.6	99.0	109.1	98.5	96.9	96.9	95.9
100	100.4	99.7	99.1	102.3	99.2	99.5	100.0	98.4

Stable Cadmium has no influence on the ^{111}In recovery and thus the reusability of the columns. The results are overall very satisfying with recoveries of 95-100% were found. In terms of ^{111}In recovery each Ln or Ac column can thus be used up to 8 times even may be more.

4.4.2 Influence of trace metal impurities and stable Cd

As already noted, after bombardment Cadmium target, ^{111}In must be separated, from target material and/or any trace elements such as Cu, Fe and Al, which could interfere in the labelling process. In order to evaluate the performance of the developed method and it's chemical purity, the influence of other metal impurities in Indium recovery as well as the content of these elements in Indium fraction were examined. Separation procedures for solutions spiked with high amounts of several elements were performed on Ln Resin® and Ac Resin® under the same conditions. These resins were found to be best suited for ^{111}In separation. The quantification of the trace elements (Fe, Cu and Al) was performed by inductively coupled plasma/optical emission spectrometry (ICP-OES).

4.4.2.1 Metal trace standards and blank calculation

The measured content of trace metal standards (A0) and blank samples which were obtained from ICP-OES measurements (see chapter 3.3.8.1) are illustrated in Table 9.

Table 4-9: Element contents in the sample loading solutions (A0) and in the blank-samples determined via ICP-OES

Sample	Al (avg) ppm	Fe ppm	Cu ppm
A0	47.5275	46.7750	48.3600
B(VC-500mg)	0.3585	0.1760	0.2675
B(VC-100mg)	0.4509	0.1831	0.2515
B(HCl 1M)	0.2510	0.2329	0.3029
B(HNO ₃ con)	0.8385	0.3195	0.2980
Average (B)	0.47	0.23	0.28

Where:

A0, is the concentration of the metal in the standards

B, is the sample blank

VC, is the amount of ascorbic acid added to the samples.

4.4.2.2 Quantification of metal impurities

The quantification of metal traces in the Indium elution steps (rinsing with HCl 6M-- 3.3.8.1.1), are illustrated in table 10. The results show that the method effectively separates ¹¹¹In from a solution which contains a large amount of impurities such as Fe, Cu and Al (1mg) and a large amount of Cadmium (100mg). Literature shows that after end of the bombardment (EOB) of Cadmium targets by protons and/or deuterons via cyclotron. The amount of these metal impurities (contaminants) what is expected in real samples are much lower than the amounts added to the samples in these experiments /Das96/ Bro71/ Mac/74/.

Table 4-10: The corporative study for the recovery (R_{mt} in %) of metal traces standard (A0) at each ^{111}In separation fractions

S is sample loading, W1 and W2 are the wash steps with HCl 0.1 and 1 M for Ln and Ac resin respectively, E is the ^{111}In -fraction (rinsing In with HCl 6M) and A0(elements) / %, are the percentage of elements (Fe, Al and Cu) found in each of the examined fractions.

Packed column	Ascorbic acid added	Sample name	A0(Al) / %	A0(Fe) / %	A0(Cu) / %
Ln	0 mg	S	81.18	7.61	90.44
		W1	11.85	24.21	11.22
		W2	0.00	2.91	<LD
		E	10.53	48.52	<LD
Ln	100 mg	S	78.52	99.64	94.86
		W1	13.35	11.33	15.20
		W2	2.14	0.08	0.00
		E	15.17	0.08	<LD
Ln	500 mg	S	85.32	99.21	73.18
		W1	10.14	9.26	18.35
		W2	1.33	0.07	7.53
		E	17.33	0.06	<LD
Ac	0 mg	S	66.14	0.00	75.89
		W1	22.31	0.12	32.69
		W2	0.04	<LD	<LD
		E	0.13	<LD	<LD
Ac	100 mg	S	80.23	77.08	62.62
		W1	18.42	27.27	43.50
		W2	0.01	<LD	0.10
		E	<LD	<LD	<LD
Ac	500 mg	S	80.59	80.24	62.05
		W1	22.05	27.89	43.83
		W2	0.00	<LD	<LD
		E	0.00	<LD	<LD

Different amounts of ascorbic acid were added to the sample loading to reduce Fe^{+3} to Fe^{+2} . For Ln Resin it is necessary to add at least 100 mg ascorbic acid to reduce Fe^{+3} to Fe^{+2} , but for Ac resin reducing Fe^{+3} to Fe^{+2} is not a problem. See Table 4-10. All experiments have been done two times and the average of each step is shown in table 4-10. The extraction and or elution behaviour of Fe, Al and Cu on Ac and Ln Resin® with different concentration of HCl are summarized in table 4-10.

The elution step E is the most important fraction in our elution study, since it represents the desired ^{111}In fraction. Reaching high yields of ^{111}In with a high chemical purity meaning very low concentration of unwanted elements (preferably concentrations below the limit of detection ~ 0.00 ppm) is a very important aspect of this project.

As can be seen in table 11, the levels of Cu, Fe and Al were found to be below 0.15 ppm in the ^{111}In fraction obtained via Ac Resin®. Hence, suitability of Ac Resin® for medical purposes was substantiated given the fact that unrealistically high concentrations of trace elements were used for the test. For the Ln Resin an insufficient separation of Al and Fe^{+3} was found. The latter problem could be resolved using a reducing agent, namely a minimum amount of ascorbic acid.

With respect to these results Ac Resin should preferably used, when high amounts of Al and Fe^{+3} are expected, the Ln Resin might then be used for a final purification of the resulting eluate, after the addition of a reducing agent.

Table 4-11: Trace elements contamination (% of Standards) on HCl (6M), stripping step for Ln Resin® and Ac Resin®

Stripping step for Ln Resin®				Stripping step for Ac Resin®			
Ascorbic acid (mg)	Al	Fe	Cu	Ascorbic acid (mg)	Al	Fe	Cu
0	10.53	48.52	< LD	0	0.13	< LD	< LD
100	15.17	0.08	< LD	100	< LD	< LD	< LD
500	17.33	0.06	< LD	500	0.00	< LD	< LD

4.4.2.3 Yield of the ^{111}In extraction

In order to determine the yield of the ^{111}In separation under the conditions given above, elution studies were performed as described in chapter 3.3.9. Possible contaminants such as Cadmium (stable or radioactive, if present), Al, Cu or Fe are removed from the column during rinsing with a total of 10 mL HCl 0.1M and 1M for Ln Resin® and /or Ac Resin® respectively, while ^{111}In retention on the columns

under these conditions is very good (see chapter 4.2.2.2). ^{111}In is removed efficiently from the column by elution with 10 mL HCl 6M. A chemical yield in the order of 85%, in presence of high amounts of metal contaminants, was obtained on both resins (see table 4-12). As was shown before, higher yields can be obtained when lower amounts of contaminants are present. In further tests, concerning reproducibility and repeatability of the separation, the amount of contaminants added to the samples were lowered.

Table 4-12: The yield of ^{111}In extraction

Fraction	Indium yield / % Ln resin	Indium yield / % Ac resin
W1	0.2	0.3
W2	0.4	0.4
E	85.9	85.4

Where :

W1, first wash step with 5 mL HCl 0.1M (Ln-resin) and 1M (for Ac-resin)

W2, first wash step with 5 mL HCl 0.1M (Ln-resin) and 1M (for Ac-resin)

E, is the elution step with 10 mL HCl 6 M

4.5 Simulated experiment

4.5.1 ^{111}In Recovery

A combination of Ln and Ac Resin® were found to provide the best conditions to perform the desired separation. Table 4-11 illustrated that in presence of high amounts of Al and Fe⁺³, Ln Resin yields insufficient separation. This problem could be solved redoing the separation procedure using Ac Resin afterward. Ac Resin

extracts Indium and separates it even from Al. Ln Resin can not achieve that. Ln Resin is used for final purification in order to obtain necessary decontamination factors. As described in chapter 3.3.10, the two resins were used successively. The eluate from the Ac column after conversion to a suitable state was used as a sample loading solution for the Ln column. The results are shown in Table 4-13.

Table 4-13: ^{109}Cd elution and ^{111}In elution

$^{109}\text{Cadmium}$ elution		$^{111}\text{Indium}$ elution	
Sample name	Cd-109 Standard [%]	Sample name	In-111 Standard [%]
S (Ac Resin)	80.69	S (Ac Resin)	0.16
W1(Ac Resin)	22.19	W1(Ac Resin)	0.13
W2(Ac Resin)	0.41	W2(Ac Resin)	0.12
S (Ln Resin)	< LD	S (Ln Resin)	0.21
W1(Ln Resin)	< LD	W1(Ln Resin)	0.16
W2(Ln Resin)	< LD	W2(Ln Resin)	0.16
E (Ln Resin)	< LD	E (Ln Resin)	75.29

Where:

S (Ac Resin) and S (Ln Resin) are sample loading solutions,

W1 and W2 are washing steps with 5 mL HCl 0.1M (LN resin) and 1M (for Ac Resin)

E is the ^{111}In fraction with HCL 6M.

Table 4-13 (left side) shows that Cd can be quantitatively washed from the Ac Resin with less than 10 mL HCl (1 mol/L); no ^{109}Cd could be detected in the final eluate E (Ln Resin), which corresponds to the In fraction. The elution study using ^{111}In shows on the other hand, that virtually no In is lost during loading and rinsing steps, resulting in an ^{111}In recovery greater than 75%.

This lack of percentage in ^{111}In recovery is because of the absorption of some activity on the beakers (glass and/or TE) during the evaporations and also a little (less than 3-4 %) will stay on the columns (Ac as well Ln columns). At Jülich ^{111}In

recovery was more than 97%. The higher yield of ^{111}In was due to the absence of losses occurring during evaporation of samples after separation steps and use of appropriate vials for LSC which also result in ^{111}In losses. At Jülich, the ^{111}In fractions are easily counted just after separation by HP-Ge detector.

The results shown in table 4-13 (right) were obtained from solutions containing 1mg/L of Al, Cu and Fe and very large amount of stable cadmium, resulting in only 75% ^{111}In recovery. As explained in chapter 4.4.2.3, the amount of metal impurities added to the samples is higher than expected in real samples. Another way to improve In recoveries would be to increase the elution volume of the Ac resin from 10 to 15 mL 6 M HCl. (last step 3.3.9.1). It can be said that the ^{111}In can be eluted quantitatively from Ac Resin however as explained some activity loss occurs during preparation and use of appropriate vials for LSC. Also, less than 5% (as explained above) will stay on the columns that can be washed with an increase in the elution volume.

4.5.2 Cd Decontamination Factor (D_f)

Cd decontamination factors were determined for the different separation steps, the results are given in table 4-15. As can be seen from S (Ln) there is no cadmium contamination left on ^{111}In fractions. Preparing the samples and experimental conditions for all of these steps were described at chapter 3.

Table 4-14: D_f of ^{109}Cd on ^{111}In extraction fractions

Separation step	Cd decontamination factor
S(Ac)	1.2
W1(Ac)	4.5
W2(Ac)	570.12
S(Ln)	8975.41
W1(Ln)	6659.89
W2(Ln)	13841.75
E(Ln)	16980.69

Where:

S(Ac), is sample loading on Ac-column

W1(Ac), is the first wash step Ac-column

W2(Ac), is the second wash step Ac-column

S(Ln), is the stripping step on Ac-column as sample loading on Ln-column

W1(Ln), is the first wash step Ln-column

W2(Ln), is the second wash step Ln-column

E is the ^{111}In stripping step (HCl 6M)

As can be seen on table 4-14 the D_f value for step E (^{111}In fraction) is very high, meaning that the In/Cd separation is working well.

4.6 ^{109}Cd recovery

Highly enriched ^{112}Cd , which is often used as radiation target is expensive. Accordingly it's quantitative recovery and subsequent clean-up for further use is of high importance.

In order to find the best suited conditions for Cd-recovery and purification several D_w measurements and elution studies were performed using TEVA Resin (pre-packed columns) and different acid concentrations (see chapter 3.4.1). Aim of these experiments was to evaluate the selectivities for ^{111}In , ^{109}Cd and as well as towards unwanted trace elements.

4.6.1 D_w values, TEVA Resin®

Figures 1-5 (see chapter 4.1) show that in general HCl and HBr are suitable media for In/Cd separation on TEVA-Resin®. In order to state the results obtained in former experiments (see chapter 4.1) additional experiments were performed; for HCl in the concentration range from 10^{-5} to 10 M, for HNO_3 and H_2SO_4 in the range of 10^{-3} to 10^1 . The results are shown in the figures 4-27 to 4-29. The obtained results are comparable to the results obtained before (see figures 1-4 chapter 4).

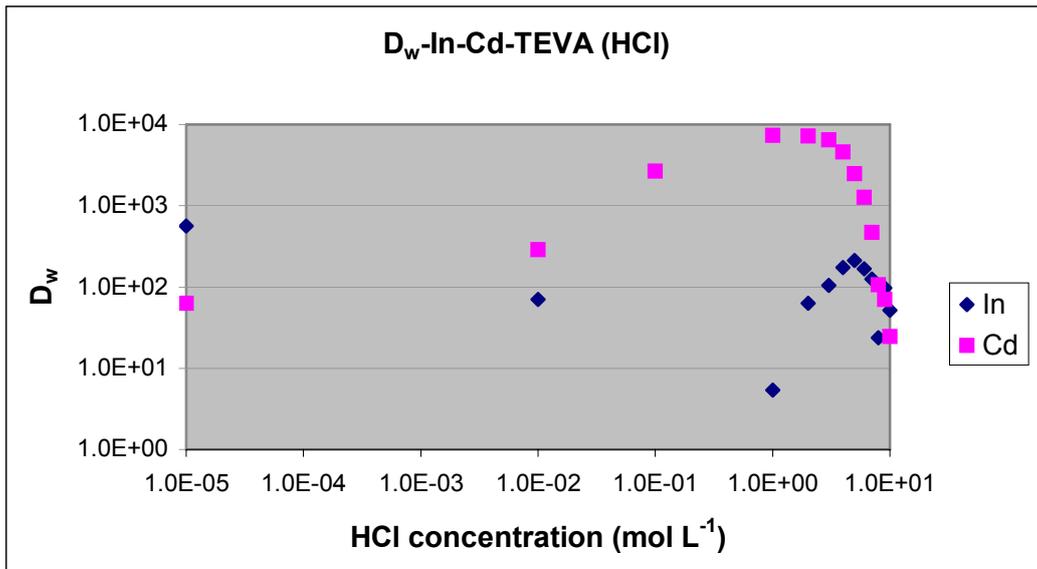


Fig. 4-27: D_w-values for In and Cd with different HCl concentrations

Fig 4-27 shows that D_w-values are rather low for both dilute HCl (Ph 5) and highly concentrated HCl (9-10 M). Therefore, these concentrations could be a used as stripping conditions.

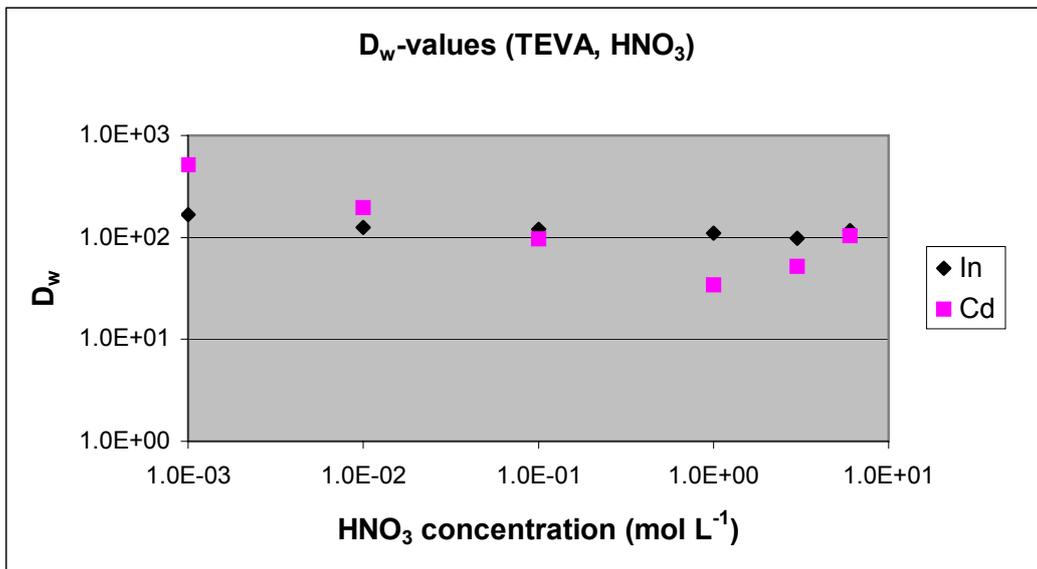


Fig 4-28: D_w-values In and Cd for TEVA Resin with different HNO₃ concentrations

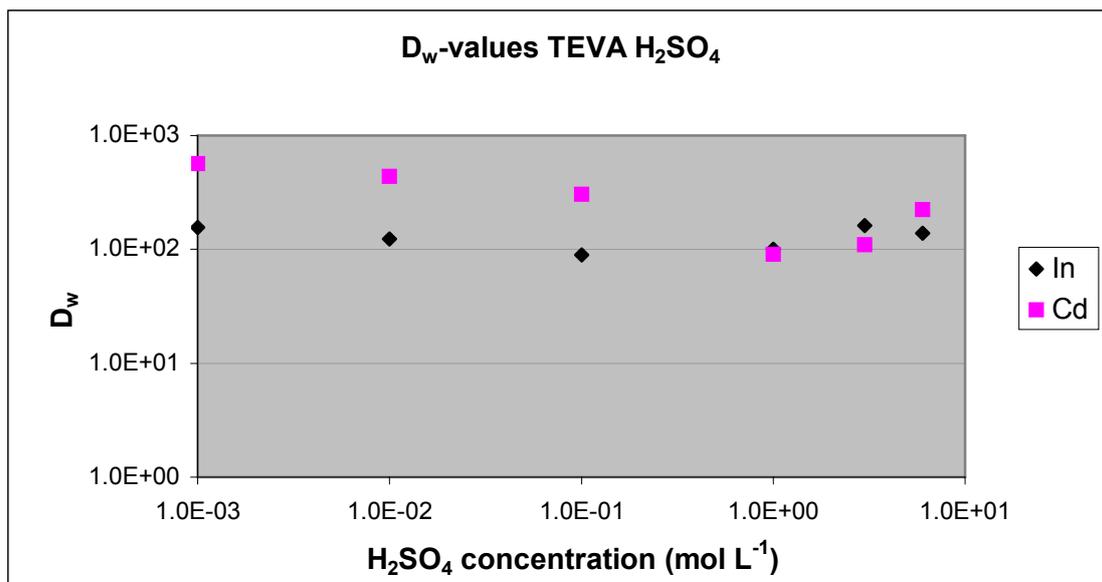


Fig 4-29: D_w-values In and Cd for TEVA Resin with different H₂SO₄ concentrations

As can be seen in figures 4-28 and 4-29 the D_w values of Cd and In are very similar over the entire acid concentration range. Hence, lack of suitable conditions for elution study when H₂SO₄ is used.

An additional experiment was performed in order to compare the D_w values of In and Cd for 0,1 and 2 M HCl on TEVA Resin® (Fig. 4-30).

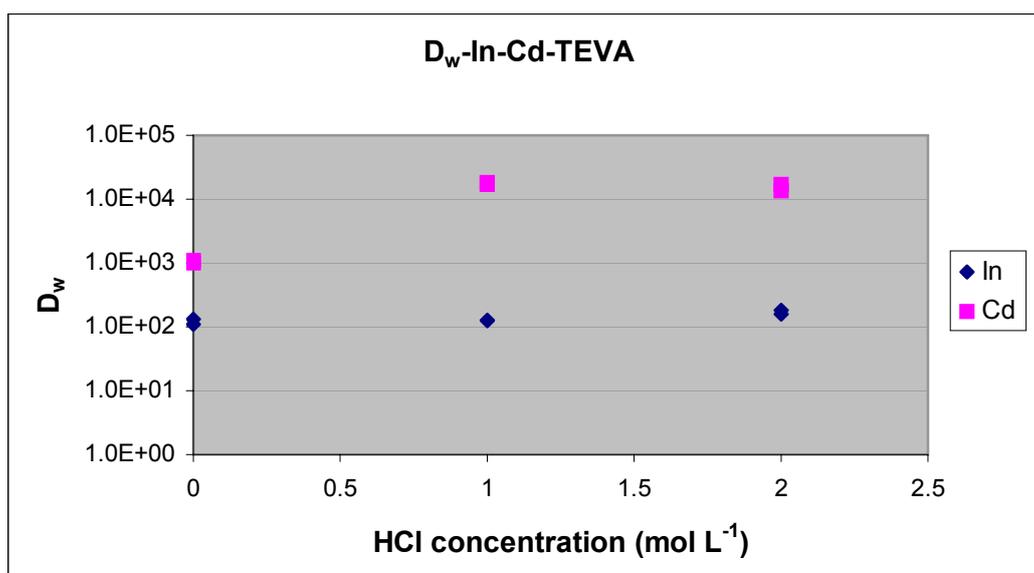


Fig 30: Comparative D_w values with HCl 0.1 and 2 M

As was expected from former results, HCl concentrations of 1 and 2 M allow a separation of Indium and Cadmium (see Fig. 4-30). One advantage of using the TEVA Resin under these conditions is, that ^{109}Cd D_w values are much higher than the ^{111}In D_w values. This means that is possible to wash ^{111}In from the TEVA columns leaving Cd on TEVA columns.

In order to evaluate ^{109}Cd stripping conditions, ^{109}Cd D_w values were determined for very low HCl concentration and distilled water, the result are compared in Table 4-15.

Table 4-15: Comparison of Cd D_w -values on TEVA Resin® for water and diluted HCl

Sample	Conc. (HCl) /M	Dw-Cd	Sample	Conc. (HCl) /M	Dw-Cd
1	0	50.2	1	1.0E-05	46.0
2	0	47.2	2	1.0E-05	52.9
3	0	47.9	3	1.0E-05	56.2

Table 4-15 shows that there is no significant difference in the results obtained with diluted HCl and water. The obtained D_w -value of about 50 is still rather high indicating that large volumes of the eluent would be needed to quantitatively elute Cadmium under these conditions. Accordingly these conditions are not considered suitable.

4.6.2 Elution study (TEVA—prepacked columns)

As described in (chapter 3.3.2) several elution studies with HCl of different concentrations (0.3 and 9 M) were performed on prepacked TEVA columns to study the elution behaviour of the ^{111}In and Cd cations. The R_{In} (in %) and R_{Cd} (in %) of the used radioisotopes were calculated using equation 3-3. The results are shown in figures 4-31- 4-33.

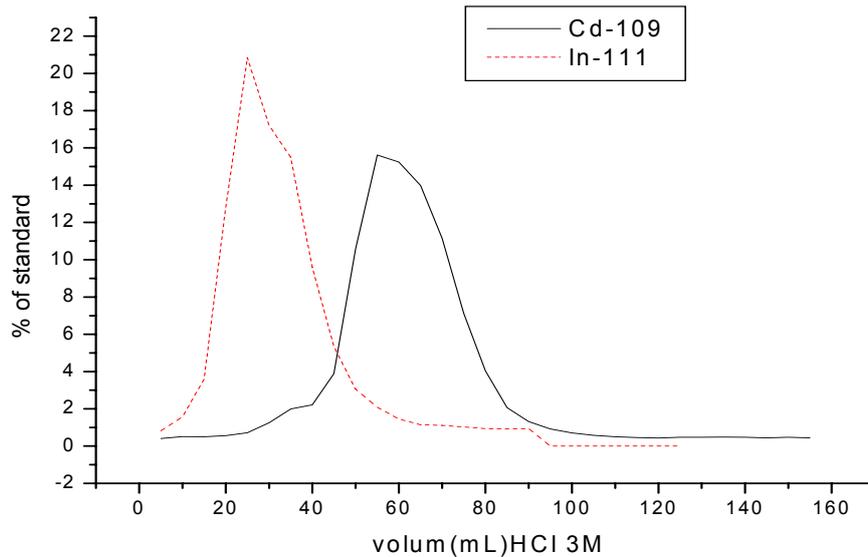


Fig 4-31: Elution behaviour for ^{111}In and ^{109}Cd on HCl 3M

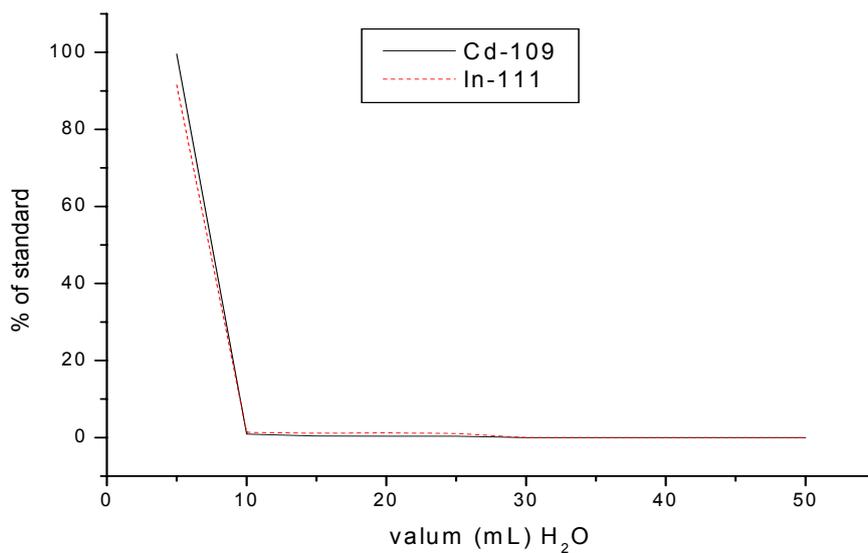


Fig 4-32: Elution behaviour for ^{111}In and ^{109}Cd on H₂O

With water and dilute HCl, ^{111}In as well as Cd can be easily removed from the TEVA columns. Although this is not a suitable condition for In/Cd separation, it is very suitable for Cd recovery.

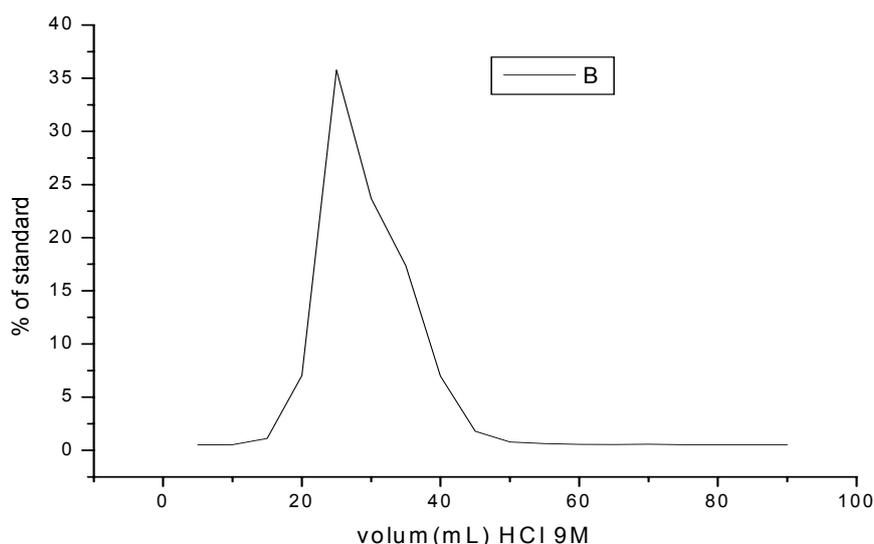


Fig 4-33: Elution behaviour of ^{109}Cd on HCl 9M

As can be seen in figure 4-32 ^{111}In and ^{109}Cd are washed easily from the TEVA columns using approximately 10 mL of water and is thus, contrary to results obtained before well suited as elution agent for Cd, in case that In was previously removed. Former investigations on TEVA Discs® showed that, Cd can also be washed easily from the TEVA columns by aqueous solutions of EDTA.

4.6.3 Cd elution using EDTA-solution

It was found that aqueous solutions containing rather large quantities of EDTA and hydrochloric acid concentrations greater than 0.1 mol L^{-1} are able to remove Cd from the TEVA Disc® (see chapter 4.1.2, figures 4-11 and 4-12). Therefore several D_w values and elution studies were performed using prepacked TEVA columns. The conditions chosen for these studies were; 2M HCl for In/Cd separation and EDTA-solutions in very dilute HCl for Cd recovery. For additional details see 3.4.3 in chapter 3.

Table 4-16: The percentage of ^{109}Cd standard in elution by EDTA-solution

Sample	Cd recovery / %		
	Exp. 1	Exp. 1	Exp. 1
S(2.5mLHCl)	0.01	0.0	0.0
W(EDTA)1	95.78	98.9	98.6
W(EDTA)2	1.00	0.2	0.4

Where:

S is sample loading (100µL Cd-109 added 0.5mg/mL Trace metals and 10 mg/mL stable Cd in 2.5 mL 2M HCL).

W(EDTA)1 is the wash step with 5mL EDTA 0.1M(in HCl 0.1 M).

W(EDTA)2 is the second wash step with 5mL EDTA 0.1M (in HCl 0.1M).

Table 4-16 shows the Cd elution behaviour using solutions of EDTA. As can be seen, ¹⁰⁹Cd recoveries are near quantitative (96 – 99 %).

4.6.4 Influence of stable contaminants on Cd recovery from TEVA column

Several elution studies were performed in order to evaluate the influence of macro amounts of stable elements on ¹¹¹In separation and ¹⁰⁹Cd recovery on TEVA-prepacked columns. The contaminants used in this case were stable Cadmium and trace amounts of Fe, Cu and Al.

The results are illustrated in table 4-17.

Table 4-17: ¹¹¹In and ¹⁰⁹Cd-recoveries on TEVA column in presence of high amounts of stable contaminants

Sample	In recovery %	Cd recovery %
S1	81.89	45.08
S2		
S3		
W1-1	10.37	31.67
W1-2		
W1-3		
W2-1	0.00	0.85
W2-2		
W2-3		
water1-1	0.86	4.32
water1-2		
water1-3		
water2-1	0.25	3.05
water2-2		
water2-3		
water3-1	0.1	2.19
water3-2		
water3-3		

Where;

S1-S3: sample loading

W1-1 to W2-3: wash steps with 5 mL HCl 2 M.

Water 1-1 to Water3-3: wash steps with 5 mL water.

Table 4-17 illustrated that, high concentration of stable Cd and a large amount of stable Fe, Cu and Al cause difficulties in the separation procedure. ^{111}In as well ^{109}Cd will break through already during sample loading and first rinsing. The amount of Cd to be recovered has to be restricted to about 10 mg, otherwise bigger columns (with higher Cd capacity) will have to be used.

4.6.4.1 Influence of varying amounts of stable impurities

To determine the maximum acceptable amount of interfering elements and stable Cadmium; i.e., in order to identify capacity of Cadmium for TEVA column in the sample loading, solutions containing ^{109}Cd or ^{111}In and varying amounts of stable Cadmium (from 0.1 to 100 mg) and possible interfering trace metals (Fe, Al and Cu) from 0.1 to 1 mg (total) were prepared. For these solutions ^{111}In or ^{109}Cd recoveries were determined. The results are summarized in tables 4-18 and 4-19.

Table 4-18: Influence of different stable interferences on ^{109}Cd -recovery

Amount of stable Cd added / mg	Amount of trace metals added / mg	^{109}Cd breakthrough %
100	0	71.4
100	0.1	62.3
100	1	76.0
50	0.1	48.5
50	0.5	40.3
10	0.1	0.1
10	0.5	0.8
1	0.1	0.1

Table 4-19: Influence of different stable interferences on ^{111}In -recovery

Amount of stable Cd added / mg	Amount of trace metals added / mg	^{111}In breakthrough %
100	0.1	92.3
100	1	103.7
50	0.5	93.4
10	0.1	0.4

The breakthrough is defined as the percentage of the respective element found in the combined sample loading and the first rinsing solution.

With increasing amounts of stable Cd the ^{109}Cd -breakthrough increases up to 76% for 100 mg of Cd. For 50 mg a breakthrough in the order of 40 – 50% is found. For 1 and 10 mg of stable Cd no significant breakthrough is found. The prepacked TEVA Resin can thus be used to purify up to 10 mg of Cd. Table 4-19 also shows that the influence of the trace metals for the given amounts of up to 1 mg, is negligible. Fig. 4-34 shows the influence of the stable Cd on the Cd breakthrough.

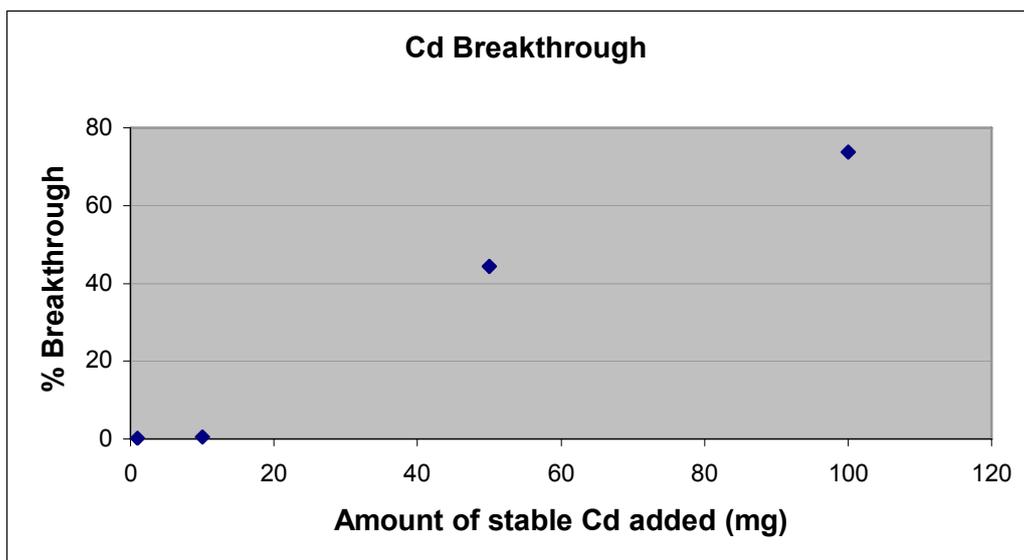


Fig 4-34: Influence of different amount of inactive Cd on ^{109}Cd -breakthrough

4.6.5 ^{109}Cd recovery and ^{111}In separation, TEVA column

With respect to information found in literature /San96, Das97/ it is to be expected, that the amount of stable impurities in the dissolved Cd-targets, as well as the mass of stable Cd used for the irradiation, should be clearly lower than the amounts added to the samples loading solution used in this work. Tables 4-19 and 4-20 show that the capacity of prepacked TEVA columns were suitable for the recovery of Cd from samples containing stable Cd in the order ≤ 10 mg and metal impurities ≤ 0.5 mg (Fe, Cu and Al). Table 4-20 summarizes the results of experiments performed using the best suited conditions for In separation and Cd recovery (see chapter 3.4.3.2.1).

Table 4-20: Elution behaviour on TEVA column for ^{111}In -separation and ^{109}Cd -recovery

$^{109}\text{Cadmium}$			$^{111}\text{Indium}$		
Sample	CPM	^{109}Cd recovery / %	Sample	CPM	^{111}In recovery / %
S	78.00	0.40	S	71.00	0.09
W1	83.80	0.43	W1	230.90	0.30
W2	72.20	0.37	W2	1065.80	1.37
Water1	105.,10	0.54	Wat1	80589.90	103.29
Water2	472.70	2.41	Wat2	1508.50	1.93
EDTA1-1	17895.30	91.16	EDTA-1	----	----
EDTA1-2	145.00	0.74	EDTA-2	----	----

Where;

S: sample loading solution (100µL ¹¹¹In and /or ¹⁰⁹Cd +10mg stable Cd + 0.1 mg trace metals (Fe, Al, and Cu)).

W1-2: HCl wash step (5mL HCl 2M).

Water 1 and water 2: water wash step (5mL deion. water).

EDTA-1 and 2: Cd elution steps with EDTA (0.1M EDTA in 0.1M HCl).

Table 4-21 shows that within 10 mL of 2M HCl ¹¹¹In and ¹⁰⁹Cd were not significantly eluted, whereas with 10 mL of water less than 2% of the ¹⁰⁹Cd were eluted, while ¹¹¹In was removed quantitatively (100%). Cd can then be eluted using 10 mL of the EDTA solution.

(Adding metal impurities to the sample loading will have some influence on the In and or Cd recovery when TEVA resin is used).

4.6.5.1 Reuse of TEVA columns for Cd recovery

A study was performed in order to estimate, if a TEVA column can be used several times. One column was thus used consecutively 6 times for Cd recovery experiments (see chapter 3.4.3.3). The Cd recoveries obtained for each of the replicates are shown in table 21.

Table 4-21: Reuse of TEVA columns for Cd recovery

Replicate	Cd-recovery (%)
1	97.2
2	96.0
3	98.1
4	95.0
5	93.1
6	93.1

The results indicate, that one column can be used up to 6 times (even more) without any impact on the Cd recovery.

4.7 The real sample experiment

4.7.1 Irradiation of the natural Cadmium

As described in chapter 3 (3.5.2) a test target (a Cd-foil with 0.125 mm thickness and 13mm diameter) was irradiated at the CV-28 cyclotron at JFZ. The activity at the end of bombardment (EOB) was about 2MBq (50 μ Ci).

After 440 minutes irradiation time the activity of real target (a seven stack Cd-foil each of 0.125 mm thickness and a diameter of 13 mm with 3 μ A and 20 MeV proton beams), at the EOB was estimated to be about 150 MBq (4 mCi) by extrapolating the former results from the test irradiation. The beam current was too high therefore the Cd foils were molten slightly together and to the Cu-foils.

4.7.2 Radioactivity determination

Fig. 4-35 shows a gamma-ray spectrum of the product 8 days after end of bombardment. The two photo peaks due to ^{111}In (171 and 245 KeV) are underlined, whereas the peak energies shown without underline are attributed to sum-coincidence (i.e. the 416 KeV) and random-coincidence or probable other radionuclides impurities such as ^{115}Cd , ^{105}Ag and $^{114\text{m}}\text{In}$. This gamma-ray spectrometry was obtained from the irradiated target solution before loading on the SPE columns (before separation), with an HPGe detector at JFZ with a relative efficiency of 30%. The counting time in this case was 5 min. A very careful search in this gamma spectrum has shown the presence of $^{114\text{m}}\text{In}$ < 5% (compared to the 171 KeV peak of ^{111}In). The ^{115}Cd and ^{105}Ag peaks were too low for definite identifications.

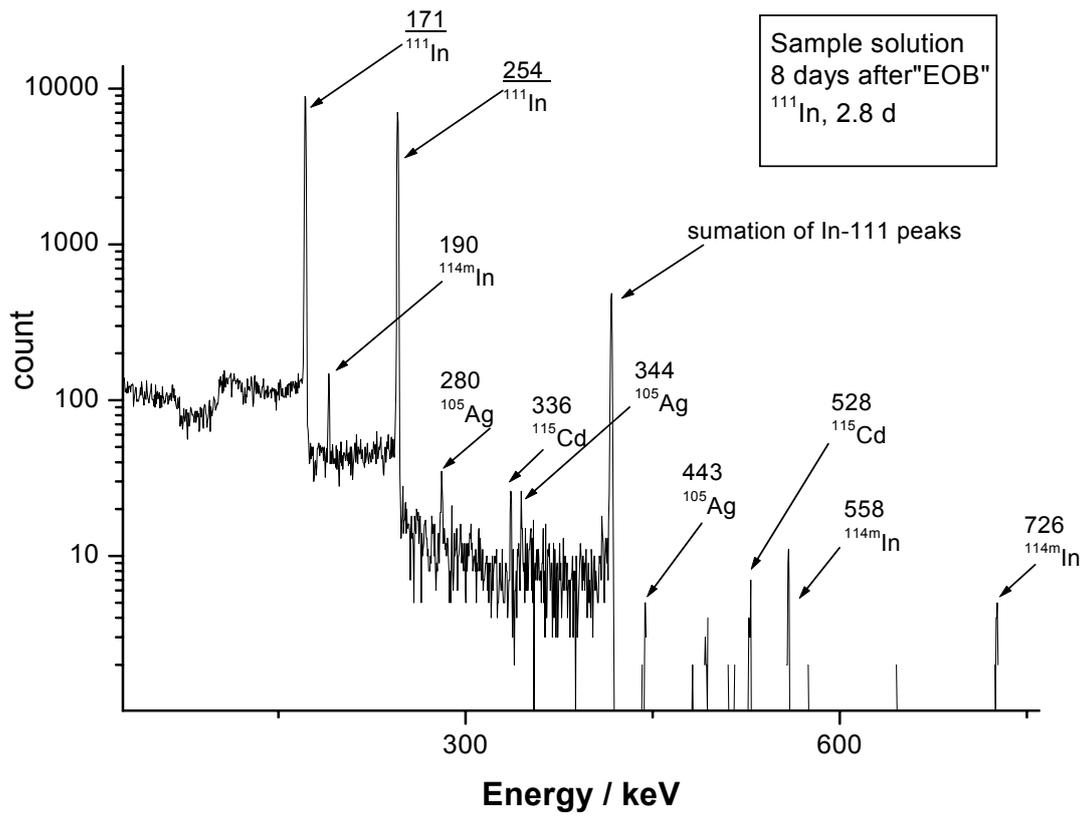


Fig 4-35: Gamma-rays spectrum of ^{111}In preparation (sample solution before loading) 8 days after the end of bombardment "EOB"

After an additional 50 d decay (see Fig 4-36) from the gamma spectrum, all three major peaks of $^{114\text{m}}\text{In}$ (190, 558 and 725 KeV), ^{105}Ag , and ^{115}Cd peaks can be readily distinguished.

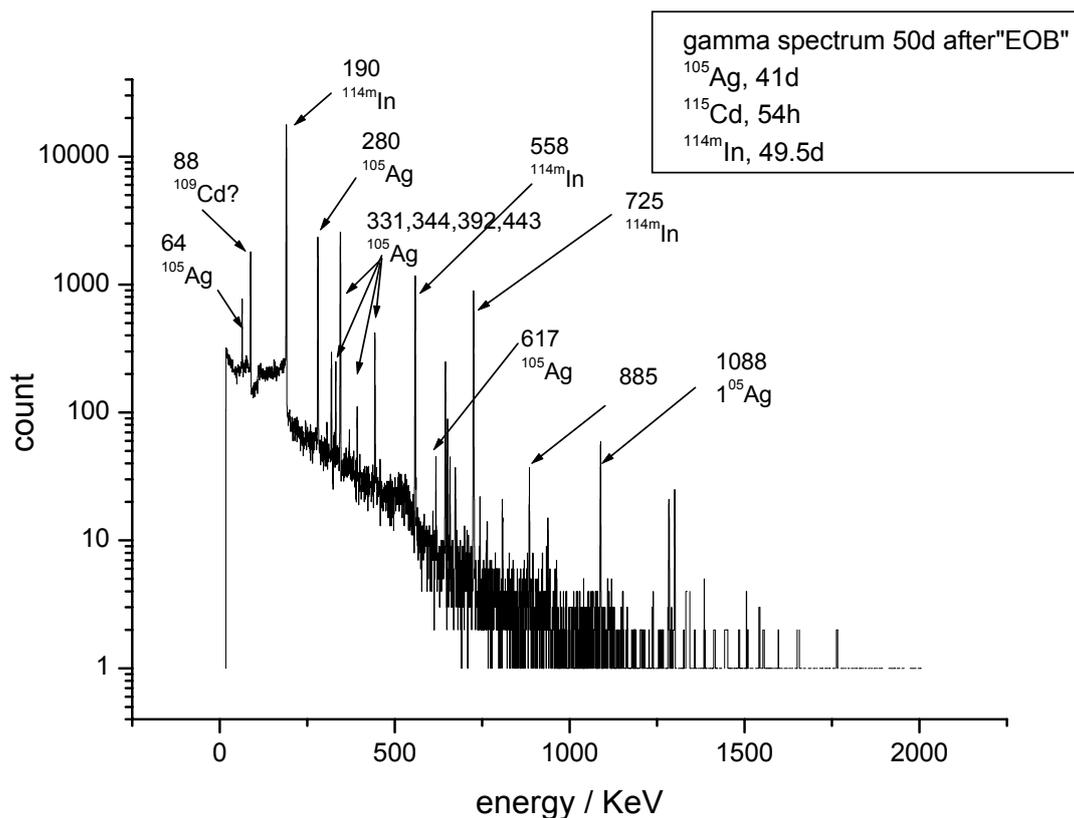


Fig 4-36: Gamma-rays spectrum of the sample solution before loading, 50 days after “EOB”

For further investigation, gamma spectra for each separation steps are shown in the appendix.

4.7.3 Separation of ^{111}In form real natural Cd targets by SPE method (TEVA, Ac and Ln resins)

The aim of this work in Jülich was to validate the separation conditions using a real irradiated cadmium target with high activity and gamma ray spectrometry. The separation conditions worked out at Marburg were used to compare the results.

4.7.3.1 Real target separation via Ac and Ln columns

In order to determine the yield of ^{111}In separation under the conditions given in chapter 3.5 for real target experiments, elution studies were performed. For Ln Resin as well as Ac Resin elution studies were performed in order to find elution volumes (rinsing), which allow high Cadmium decontamination combined with high Indium recovery. Figures 4-37 to 4-40 show the results of the elution curves performed with Ln Resin® and Ac Resin® using HCl 6M.

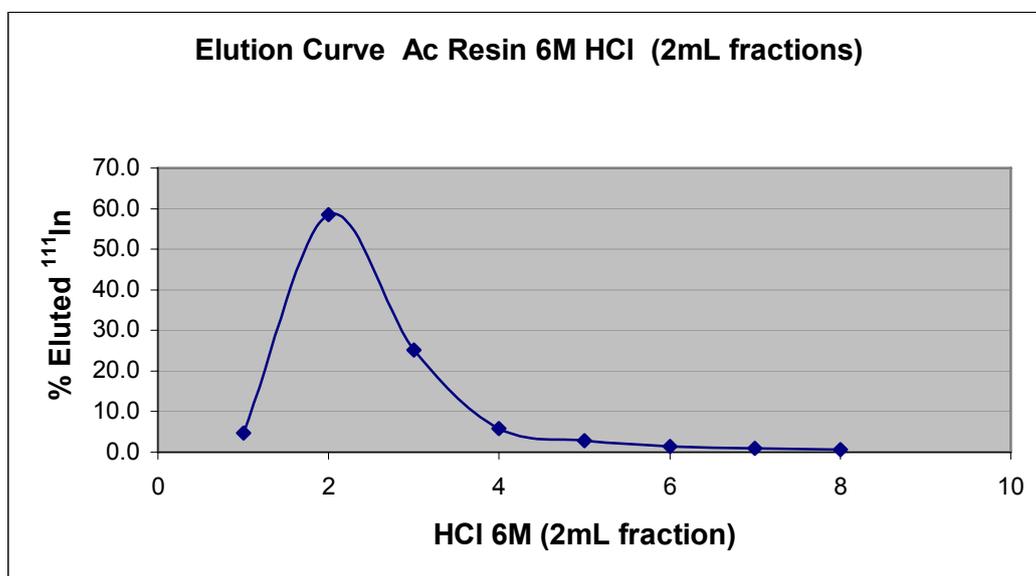


Fig 4-37: Elution study via Ac Resin® with HCl 6M ^{111}In -fractions

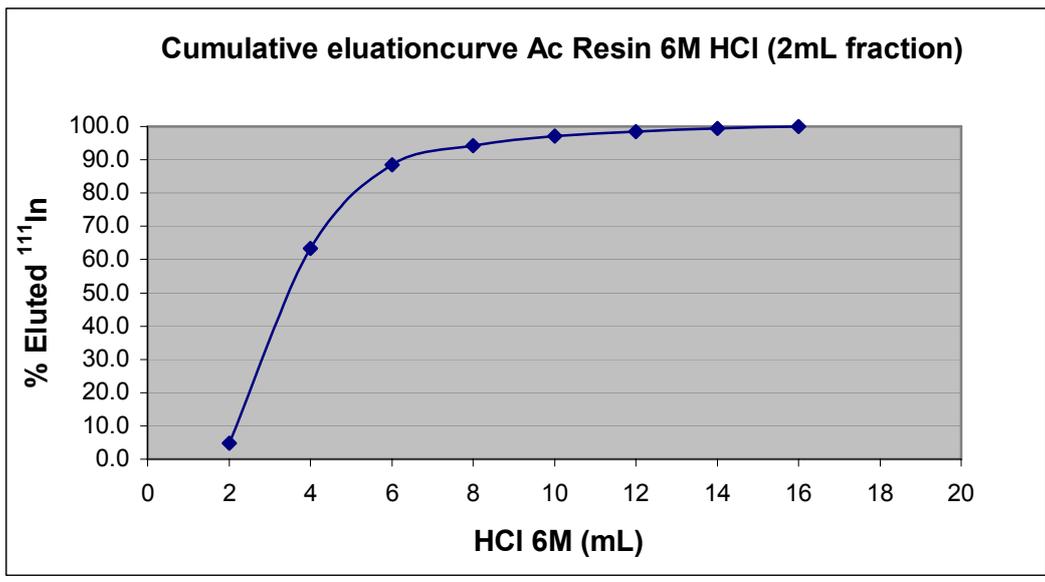


Fig 4-38: Accumulative elution curve for ¹¹¹In with Ac Resin and HCl 6M

The curve in Fig. 4-41 is shown for Ac Resin® the ¹¹¹In-recovery yield is > 97 % within 16 mL HCl 6M and the yield of 92 % within 8mL HCl 6M. The error estimation was 3-5 %.

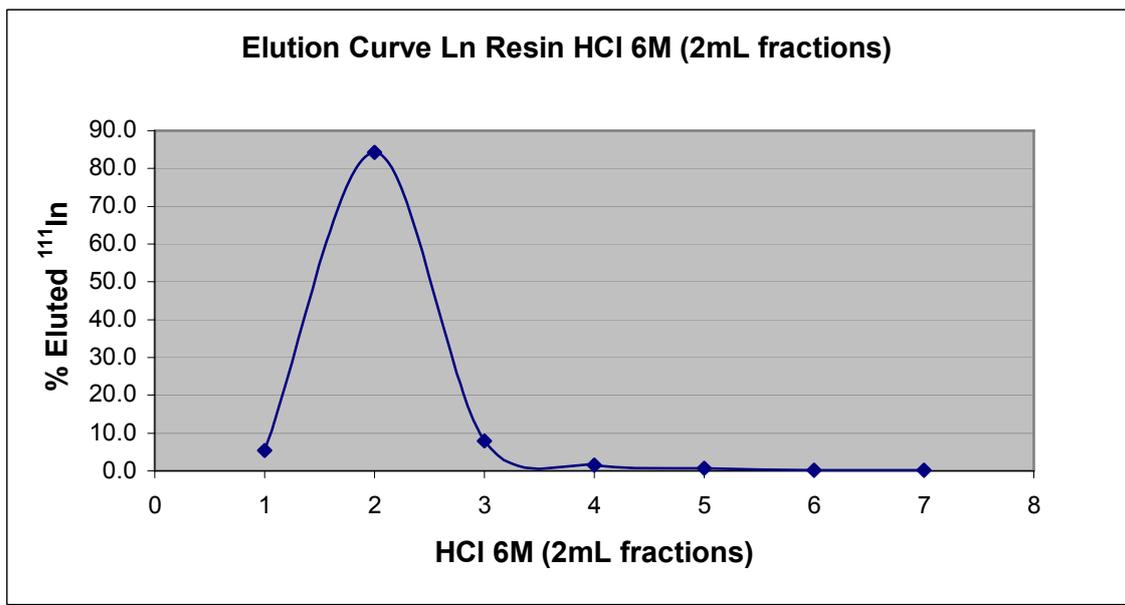


Fig 4-39: Elution study via Ln Resin® with HCl 6M ¹¹¹In-fractions

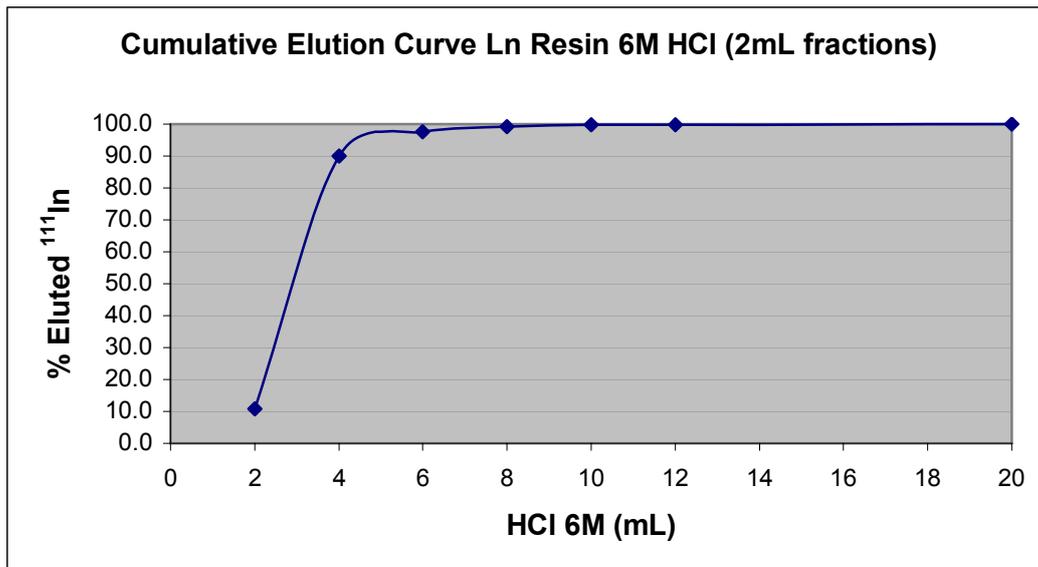


Fig 4-40: Cumulative elution curve for ¹¹¹In with Ln Resin and HCl 6M

Figures 4-39 and 4-40 (for Ln Rein®) shown the ¹¹¹In-recovery yield is > 99 % within 10 mL and the yield of 97 % within 6mL HCl 6M. The error estimation was 3-5 %.

4.7.3.2 Radioisotope impurity detection by gamma spectroscopy

Fig. 4-41 shows a gamma-ray spectrum of ¹¹¹In fraction after separation procedure via simulated experiment which is explained in chapter 4.5

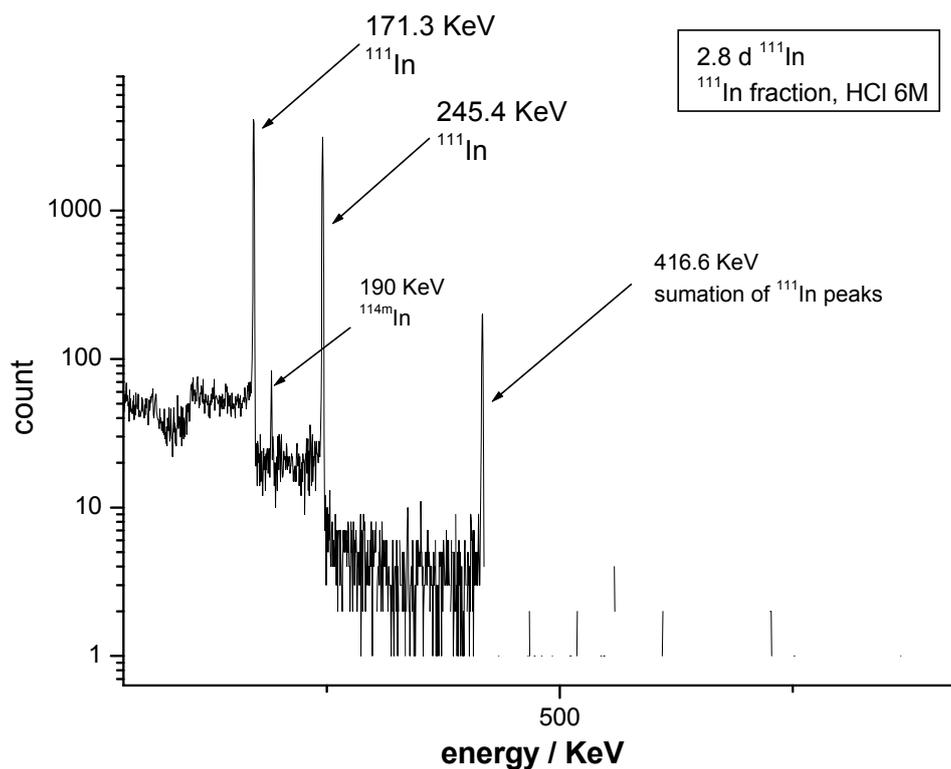


Fig 4-41: Gamma-rays spectrum of the ^{111}In fraction solution after separation procedures.

Fig. 4-41 shows in ^{111}In -fraction there was $^{114\text{m}}\text{In}$ (50 d) contamination which is only about 0.5 % of the ^{111}In activity. The simultaneous production of large amounts of this long-lived radionuclide is undesirable due to the increased radiation dose to the patient. Minimization of $^{114\text{m}}\text{In}$ in an ^{111}In preparation destination for human use is highly desirable. The $^{114\text{m}}\text{In}$ contamination could be reduced for the (p,2n) production path at the cost of lower production rates by increasing the energy of the induced protons up to 22 MeV. Further reduction of $^{114\text{m}}\text{In}$ contamination is achieved by decreasing the total target thickness and irradiating highly enriched ^{112}Cd targets via ^{112}Cd (p,2n) ^{111}In reaction. See the excitation function for the production of $^{114\text{m}}\text{In}$ in Fig. 1-1 chapter 1.7. Note in Fig. 4-14 that there were no radioisotopes of Cadmium and/or any other radioisotope impurities observed.

4.7.3.3 Real target separation via TEVA Resin®

Figures 4-42 and 4-43 show the results of the elution curves performed with TEVA prepacked columns. After loading the sample solution the column was washed with HCl 12 M up to 14 mL. All fractions (each 1 mL HCl 12 M) were counted with a HPGe detector, no ^{111}In breakthrough was absorbed. The wash steps were continued by washing fractions (2 mL HCl 2M) with HCl 2M and then were continued 2 times washing with 5 mL water.

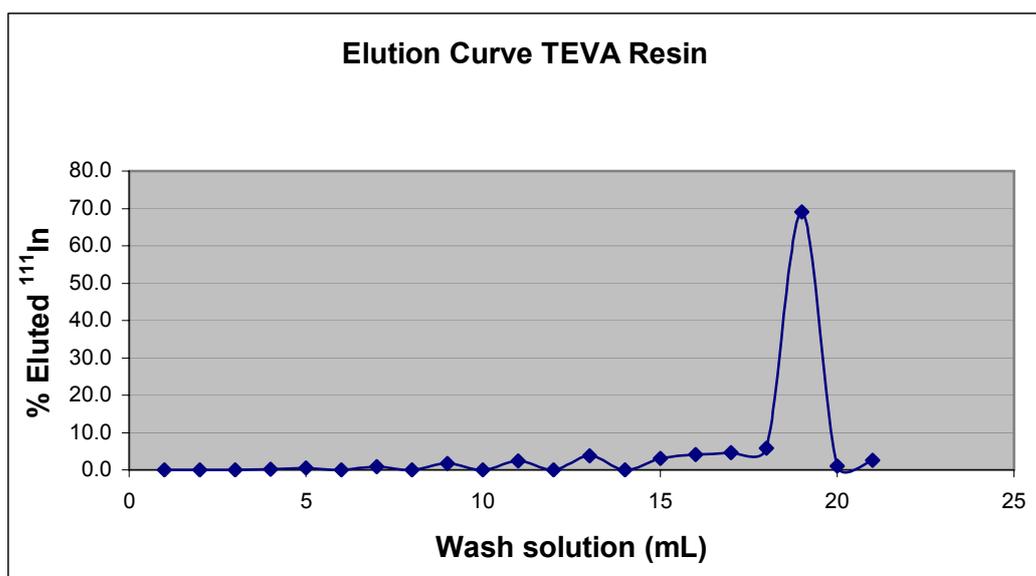


Fig 4-42: Elution study via TEVA Resin® with HCl 12M, 2M and water (^{111}In fractions)

A carefully performed gamma spectroscopy of each wash fraction showed that TEVA Resin starts to elute at about 1 % of ^{111}In loaded on column, while Cd and Ag will elute within 15 mL of HCl 12 M.

To wash the ^{111}In from the resin diluted HCl or water is needed. See the earlier results of this work in 4.2.

The overall ^{111}In -recovery was 83% - 86% in Indium fraction. See Fig. 4-43.

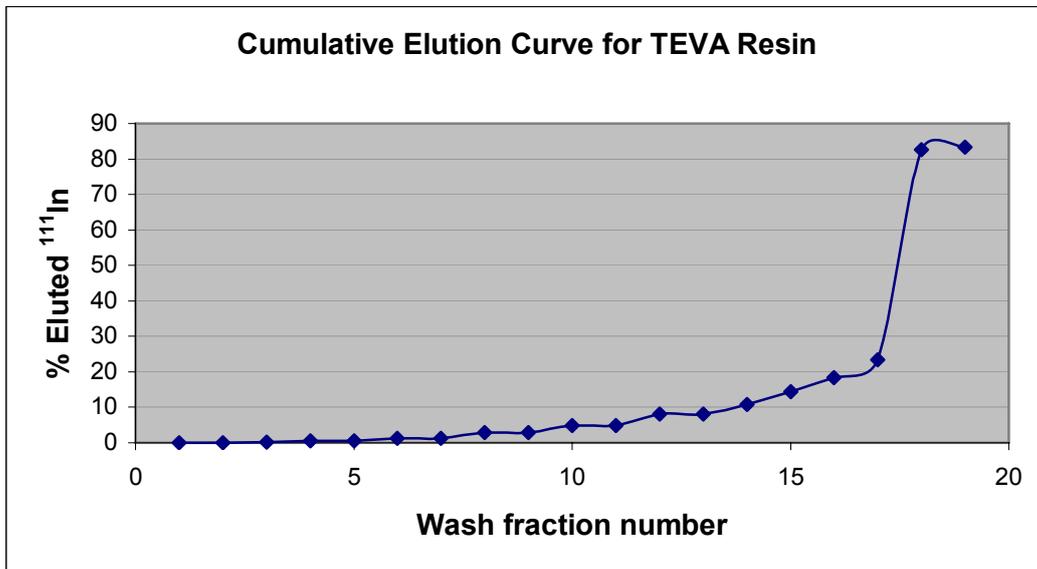


Fig 4-43: Cumulative elution curve for ¹¹¹In with TEVA Resin and HCl 2M and water

Where fraction 1 to 14 are wash steps with 1mL HCl 12 M and fractions 14 to 17 are with HCl 2M and fractions 18 and 19 are wash steps with water.

Fig. 4-44 shows the integral cumulative elution curve for the recovery activity of all fractions.

As expected from the earlier results of this work, TEVA Resin® does not exhibit favorable results for ¹¹¹In separation. A significant disadvantage of TEVA Resin® is its very low eluent velocity.

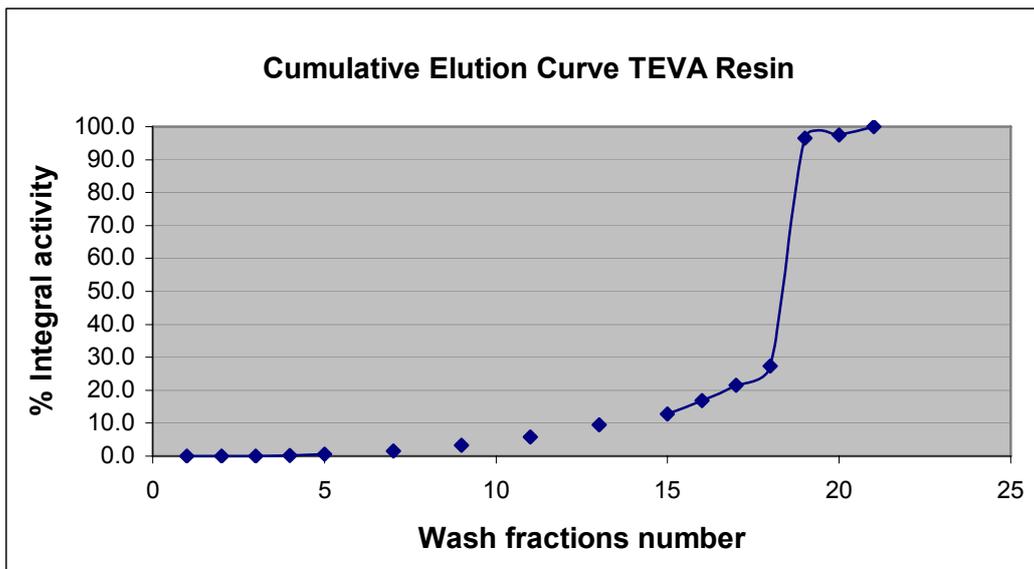


Fig 4-44: Cumulative elution curve for extraction the activity of the wash fractions with TEVA Resin

Fraction 1 to 14 are wash steps with 1mL of HCl 12M, fractions 14 to 17 are wash steps with 2 mL of HCl 2M, fractions 18 and 19 are wash steps with 5mL of water, and fraction 20 is the activity remaining on the TEVA column. Wash fraction number 14 with water and/or 2 mL of diluted HCl 2M exhibited a milky white appearance after the solution was left over night. The white colour of the solution is probably due to the deterioration of TEVA column. Washing the column 14 times with HCl 12M renders the TEVA column completely unusable.

5 Conclusion

Separation of high purity ^{111}In from irradiated Cadmium targets for medical purposes is the major aim of this work. To this end, various experiments using the Solid Phase Extraction (SPE) methods have been documented in this research. This thesis illustrates a fast and convenient way for further purification of ^{111}In solutions shortly before their use. Means of selective recovery of highly enriched ^{112}Cd from dissolved targets is also provided, since highly enriched ^{112}Cd is expensive. Weight distribution ratios (D_w values), as a measure of the distribution behavior of Indium and Cadmium on different SPE materials in different acids or acid/salt mixtures of varying concentrations have been determined to arrive at optimal conditions for separation and purification of carrier-free ^{111}In from irradiated Cadmium targets. Elution studies have been undertaken to examine the behaviour of Cadmium and Indium isotopes on four commercially available SPE materials--TEVA Resin®, TRU Resin®, Ln Resin® and Ac Resin® all of which are manufactured by Eichrom Technologies, Inc. These resins have been thoroughly examined towards their usefulness for achieving the above mentioned goals.

It was found during the course of this work that for both acids; HCl and HBr, the D_w values on TEVA Resin® show an Indium/Cadmium separation is possible. However, taking into consideration the limited capacity of the disc, separation of Indium from macro amounts of Cadmium is very difficult, if not impossible, since both cations compete for the same free active sites.

In general, Cadmium has higher distribution ratios than Indium. Conditions for the selective removal of trace amounts of Cadmium from Indium solutions were found and evaluated by determining the decontamination factors and Indium recoveries. The proposed method is accomplished within a few minutes without much effort. It is shown that by using the described separation method Indium recoveries greater than 85% are achievable while the decontamination factors for Cadmium are in the order of 10,000. The mean recovery of the ^{111}In standard was found to be 86.5 (+/- 9.2, k=1) %.

Unfortunately, the TEVA® discs showed lack of long term stability as indicated by the decrease in Cadmium D_f values. It was determined that the disc should be replaced once used in three separations. It was investigated whether EDTA solutions are appropriate to aid in Cadmium removal from the disc, and it was found that aqueous solutions containing rather large amounts of EDTA (0.5 mol L^{-1} as well as 0.1 mol L^{-1}) solutions with hydrochloric acid concentrations greater than 0.1 mol L^{-1} , give low weight distribution ratios (D_w —chapter 4, Figures 11 and 12) and might therefore be used to remove Cadmium from the TEVA Disc®.

D_w curves for Ln, Ac and TRU resins; i.e., extraction chromatographic materials based on organophosphorus chelating agents for $^{111}\text{In}/^{109}\text{Cd}$ separation, were obtained for different concentrations of HNO_3 and HCl . The corresponding values are shown in chapter 4, Figures 13-18. The best experimental results were obtained employing Ln Resin® and Actinide Resin®. Both resins were found to be well suited to separate ^{111}In from irradiated Cadmium targets. Conditions were established under which the difference in the D_w values of Indium and Cadmium were in the three or four orders of magnitude, with Indium D_w values being superior, meaning that the resins show higher selectivity for Indium. Nevertheless, there were also conditions that would allow Indium elution. HCl and HNO_3 were both found to be suitable media for the desired separation. However for further experiments, HCl was chosen with respect to the fact that HNO_3 is not considered an acceptable media for labelling reactions or medical application. This would necessitate an additional step to convert the obtained ^{111}In solution from nitrate to chloride media.

The TRU Resin® was not found to be suited for Indium/Cadmium separation and subsequent Indium elution, since differences in D_w values compared to the other two resins were considerably lower for HCl or HNO_3 .

One of the ^{111}In products in a cyclotron is $\text{Cd}(\text{p}, \text{xn})^{111}\text{In}$. In view of medical usage of radionuclides after bombardment, the produced ^{111}In must be separated from the Cadmium targets and other unwanted elements such as Cu , Fe or Al . Cadmium as well as potential impurities can be separated in a one-step procedure using the SPE technique. This work examined the impact of macro amounts of the mentioned cations on the Indium/Cadmium separation and on the Indium recovery as well as

the chemical purity of the Indium fraction. For the Ln Resin® as well as for the Ac Resin®, the influence of macro amounts of inactive Cadmium on the Indium D_w values was evaluated. Results show that ^{111}In recovery under these conditions is close to 100%. The D_f values for Cadmium on the Ln Resin® and the Ac Resin® under these conditions were also determined. The D_f values were greater than 20,000, hence the separation provided an excellent Cadmium decontamination in Indium fraction.

As expected, the elution profile on Ln and Ac resins shows that a macro amount of stable Cadmium (up to 100 mg) has no influence on the ^{111}In recovery. Additional experiments show that stable Cadmium has no influence on Indium recovery. The columns in this experiment were reused more than 8 times without any degradation in the columns effectiveness. The overall results were very good with recoveries ranging 95-100%.

In order to evaluate the performance of the developed method and the resulting chemical purity, the influence of trace metal impurities on Indium recovery as well as the content of these elements in Indium fraction was examined. Separation procedures for solutions spiked with high amounts of several elements were performed on Ln Resin® and Ac Resin® under the same conditions. These resins were found to be best suited for ^{111}In separation. Reaching high yields of ^{111}In with high chemical purity; i.e., very low concentration of unwanted elements (preferably below the limit of detection $< 10^{-8}$) was a very important aspect of this project.

The quantification of the trace elements (Fe, Cu and Al) was performed by inductively coupled plasma/optical emission spectrometry (ICP-OES). The levels of Cu, Fe and Al were found to be below 0.15 ppm in the ^{111}In fraction obtained via Ac Resin®. Hence, suitability of Ac Resin® for medical purposes was substantiated given the fact that unrealistically high concentrations of trace elements were used for the test.

For the Ln Resin® an insufficient separation of Al and Fe^{+3} was found. The latter problem could be resolved using a reducing agent, namely a minimum amount of ascorbic acid.

With respect to these results, Ac Resin® should preferably be used when high amounts of Al and Fe⁺³ are expected, whereas Ln Resin® should be used for final purification of the resulting eluate after the addition of a reducing agent. Nonetheless, a chemical yield in the order of 85%, in presence of high amounts of contaminants was obtained when both resins were used. Higher yields could be obtained when lower amounts of contaminants were present. A combination of Ln Resin® and Ac Resin® was determined to be best suited to perform the desired separation when high amounts of Al and Fe⁺³ were present as Ln Resin® alone would not yield sufficient separation. However, this deficiency can be overcome by redoing the separation procedure using Ac Resin® afterwards. Ac Resin® extracts Indium and separates it from Aluminium. Ln Resin® can not achieve that. Ln Resin® should be used for final purification in order to obtain the necessary decontamination factors. As described in chapter 3.3.10, the two resins were used successively. The eluate from the Ac column after conversion to a suitable state was used as a sample loading solution for the Ln column. This resulted in an ¹¹¹In recovery greater than 75%. The drop in ¹¹¹In recovery is partially due to some absorption activity on the beakers (glass and/or Teflon®) during the evaporations with a little less than 3-4 % activity remaining on the columns (Ac and Ln). As explained in chapter 4.4.2.3, it is emphasized that the amount of metal impurities added to the samples in these experiments was much higher than what is expected in typical samples /Das96/Bro71/ Mac74/.

Another way to improve Indium recoveries is to increase the elution volume to rinse the activity from the columns. Several elution studies were performed in order to evaluate the influence of macro amounts of stable elements on ¹¹¹In separation and ¹⁰⁹Cd recovery on prepacked TEVA columns. High concentration of stable Cadmium and large amounts of stable Fe, Cu and Al complicate the separation procedure. ¹¹¹In as well ¹⁰⁹Cd will break through readily during sample loading and initial rinsing. Unless the amount of Cadmium to be recovered is restricted to about 10 mg, larger columns with higher Cadmium capacity must be used.

With increasing amounts of stable Cadmium, the ¹⁰⁹Cd break-through increases up to 76% for 100 mg of Cadmium. For 50 mg of Cadmium a break-through in the order of 40 – 50% was found. For 1 and 10 mg of stable Cadmium no significant break-

through was found. The prepacked TEVA Resin® can therefore be used to purify up to 10 mg of Cadmium effectively. The results as indicated in chapter 4.4.4.1 also show the influence of trace metals for amounts up to 1 mg is negligible. Based on information found in literature /San96/Das97/, the expected amount of stable impurities in the dissolved Cadmium targets, as well as the mass of stable Cadmium used for irradiation, should be clearly lower than the amounts added to the sample loading solution. Tables 4-19 and 4-20 in chapter 4 show that the capacity of prepacked TEVA columns was suitable for the recovery of Cadmium from samples containing stable Cadmium in the order of ≤ 10 mg and metal impurities in the order of ≤ 0.5 mg (Fe, Cu and Al). These results indicate that one TEVA column can be used up to 6 times or even more without any impact on the Cadmium recovery.

As expected from the earlier results of this work, TEVA Resin® did not exhibit favorable results for ^{111}In separation. A significant disadvantage of TEVA Resin® is its very low eluent velocity. However, the capacity of prepacked TEVA columns was favorable for the recovery of Cadmium from samples containing stable Cadmium in the order of ≤ 10 mg with metal impurities (Fe, Cu and Al) in the order of ≤ 0.5 mg. Table 4-20 summarizes the results of the experiments using the best suited conditions for Indium separation and Cadmium recovery. Table 4-21 shows that when a total of 10 mL of 2M HCl was used to rinse the columns, ^{111}In and ^{109}Cd were not significantly eluted. When a total of 10 mL of water was added to the rinse, less than 2% of the ^{109}Cd was eluted however resulting in 100% removal of ^{111}In . Cadmium was then eluted using 10 mL of the EDTA solution resulting in full recovery of Cadmium.

The best selective separation conditions documented in this study were validated against separation conditions using a real irradiated Cadmium target at the cyclotron CV-28 at Jülich Research Center (JRC). The Cadmium target was irradiated with 18 MeV protons. The separation conditions worked out at the Nuclear Chemistry Department at Marburg Philipps University were then used to compare the results. The separation of Cadmium target material from induced n.c.a. ^{111}In (no-carrier-added) activity was highly favorable for Ac Resin® and Ln Resin®. Especially the Ln Resin® was found ideal for this separation. For Ac Resin® the ^{111}In recovery yield was better than 97% when the rinsing was done with a total of 16 mL HCl 6M. The recovery yield was 92% when the total volume of rinse was 8mL HCl 6M. For Ln

Resin® the ^{111}In recovery yield was better than 99% when the total volume of rinse was 10 mL. The recovery yield was 97% when the total volume of rinse was 6mL HCl 6M. The error was estimated to be 3-5%.

To determine the probable radiochemical impurities in the ^{111}In fractions (see Fig. 4-35), the gamma ray spectrums (of irradiated Cadmium solution) before loading on the SPE columns and ^{111}In fractions (after separation procedure) were analyzed. The gamma ray spectrum of the product 8 days after EOB showed two photo peaks due to ^{111}In (171 and 245 KeV) and other peak energies due to sum-coincidence (i.e. the 416 KeV), and random-coincidence or probable other radionuclide impurities such as ^{115}Cd , ^{105}Ag and $^{114\text{m}}\text{In}$. This gamma ray spectrometry was obtained from the irradiated target solution before loading on SPE columns with an HPGe detector at JFZ with a relative efficiency of 30%. A careful scrutiny of this gamma spectrum showed the presence of $^{114\text{m}}\text{In}$ to be less than 0.5% compared to 171 KeV peak of ^{111}In fraction. The ^{115}Cd and ^{105}Ag peaks were too low for definite identifications.

After an additional 50 d decay, from the gamma spectrum of irradiated Cadmium target, all three major peaks of $^{114\text{m}}\text{In}$ (190, 558 and 725 KeV), ^{105}Ag and ^{115}Cd could be readily distinguished.

Minimization of $^{114\text{m}}\text{In}$ in an ^{111}In fraction for human use is vital. The $^{114\text{m}}\text{In}$ contamination in the Cd (p, 2n) ^{111}In production path could be reduced at the cost of lower production rates by increasing the energy of the induced protons up to 22 MeV and decreasing the total target thickness. Reduction of $^{114\text{m}}\text{In}$ contamination can also be accomplished through irradiating highly enriched ^{112}Cd targets via ^{112}Cd (p, 2n) ^{111}In reaction.

The gamma spectrometry showed no radioisotopes of Cadmium and/or any other radioisotope impurities in the ^{111}In fractions. These results demonstrate Ac Resin® and Ln Resin® when used in the SPE method facilitate an excellent separation and purification of ^{111}In from irradiated natural Cadmium targets.

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