Radiochim. Acta **90**, 167–177 (2002)

Production of the positron emitter ^{51}Mn *via* the ^{50}Cr(d, n) reaction: targetry and separation of no-carrier-added radiomanganese

By A. T. J. Klein[1], F. Rösch[2], H. H. Coenen and S. M. Qaim*

Institut für Nuklearchemie, Forschungszentrum Jülich GmbH, D-52425 Jülich, Germany

(Received May 25, 2001; accepted in revised form August 21, 2001)

Nuclear reaction / Separation of positron emitter ^{51}Mn / Ion exchange chromatography / Solid phase extraction / Liquid–liquid extraction / Enriched target recovery

Summary. In connection with the production of 46.2 min ^{51}Mn *via* the ^{50}Cr(d, n)-process, several separation techniques such as ion exchange chromatography, solid phase extraction, liquid–liquid extraction and co-precipitation have been investigated; the aim was to separate no-carrier-added radiomanganese from the bulk target chromium. Among the separation systems *Mn^{II}/Cr^{III}, *Mn^{II}/Cr^{VI} and *Mn^{IV}/Cr^{VI}, the latter applying the co-precipitation of *Mn^{IV} with Fe^{III} hydroxide was found to be the optimum; the removal of chromium was rapid and quantitative (remaining content $< 0.05\%$) and the separation efficiency was high (99.3% radiochemical yield of *Mn). For production purposes, a sandwiched pellet of the chemical composition $Al_4 \cdot {}^{50}CrCl_3$ was developed as a new target. This allowed a quick dissolution after irradiation, thus enabling a fast separation of ^{51}Mn and its production on a MBq scale. A 1 h irradiation at 3 μA (wobbled beam) over an effective deuteron energy range of $E_d = 12.8 \rightarrow 7.9$ MeV yielded 107 MBq ^{51}Mn. Simultaneously formed nuclides of other elements, such as ^{38}Cl, ^{24}Na, ^{48}V and ^{51}Cr were quantitatively separated using the proposed procedure. Only the shorter-lived radioisotope ^{52m}Mn, formed *via* the ^{52}Cr($d, 2n$)^{52m}Mn reaction, was present at a low level of 2%, if the enrichment of ^{50}Cr was 95% (with ∼ 5% ^{52}Cr).

1. Introduction

Due to its high spatial resolution and radiation-free character, Magnetic Resonance Imaging (MRI) is finding increasing application in diagnostic medicine. Thereby, contrast can be enhanced using paramagnetic agents. Presently, the preferred contrast agents are chelated high spin metal ions such as Gd^{III} and Mn^{II}/Mn^{III}. However, exact biodistribution data and quantitative uptake kinetics of those magnetopharmaceuticals in tissues and organs are poorly known since the paramagnetic centres can only be localized indirectly by their detectable effect on water protons. An exact knowledge of pharmacokinetics in man is of strong interest regarding the optimization of those chemical compounds (drug design) and MRI protocols.

An easy access to such data could be provided by the radiolabelling technique. In case of manganese, several radioisotopes are suited because of reasonable half-lives. Production routes have been reported for ^{56}Mn (2.58 h) [1], ^{54}Mn (312.2 d) [2, 3], ^{52}Mn (5.6 d) [4, 5], ^{52m}Mn (21.1 min) *via* parent ^{52}Fe [6], and ^{51}Mn (46.2 min) [3]. In fact, radiotracers have already been used for labelling contrast agents [7–10], but due to the limiting physical properties of the nuclides used (long half-life, β^--decay etc.) only invasive animal experiments were conducted yielding pharmacokinetic data and therefrom derived organ doses. As a further step, quantitative *in vivo* data in man can be obtained *via* the non-invasive techniques Single Photon Emission Computed Tomography (SPECT) and Positron Emission Tomography (PET). While in the case of Gd-compounds the SPECT nuclide ^{147}Gd ($t_{1/2} = 38.1$ h, $E_\gamma = 229$ keV (61%)) has been shown to be suitable [11], manganese offers two PET nuclides, namely ^{52m}Mn ($t_{1/2} = 21.1$ min, $I_{\beta^+} = 97\%$, $E_{\beta^+(\max)} = 0.6$ MeV, IT $= 1.75\%$) and ^{51}Mn ($t_{1/2} = 46.2$ min, $I_{\beta^+} = 97\%$, $E_{\beta^+(\max)} = 2.5$ MeV). ^{52m}Mn of high radionuclidic purity is only available from the ^{52}Fe/^{52m}Mn generator [12–20], since direct nuclear reactions, such as the ^{52}Cr($p, 2n$) process, always lead to an isomeric mixture [3, 4]. The almost pure positron emitter ^{51}Mn in comparison has a suitable half-life and can be produced at a small cyclotron in high radionuclidic purity using the ^{50}Cr(d, n) reaction [3, 21]. After the bombardment, the generated n.c.a. ^{51}Mn should be separated with high radiochemical efficiency and speed from the bulk of the target chromium and radionuclides of other elements. However, the only chemical form of target used for ^{51}Mn production until now was Cr_2O_3 [22–27], whose dissolution after irradiation is difficult and time consuming. We searched for a new target material, which allows a fast dissolution and is well suited for the subsequent separation procedure. Besides high radiochemical purity and high radiochemical yield of ^{51}Mn, the procedure should enable a remote or automatic process control. With this aim, several different separation techniques were investigated.

*Author for correspondence (E-mail: S.M.QAIM@FZ-JUELICH.DE).
[1] Present address: Abteilung Nuklearmedizin, Universitätsklinikum Ulm, D-89081 Ulm, Germany
[2] Present address: Institut für Kernchemie, Johannes Gutenberg-Universität, D-55128 Mainz, Germany

2. Materials

2.1 Chemicals

The complexing agents acetylacetone (Hacac, pentane-2,4-dione), 2-thenoyltrifluoroacetone (H-TTA, 4,4,4-trifluoro-1-(2thienyl)-1,3-butadiene), 8-hydroxquinoline (8-Hqu, 8-quinolinol) and the ion-exchange resins, DOWEX 50W×8 and DOWEX 1×8 in different mesh sizes, were obtained in a specially cleaned grade from FLUKA, Buchs, Switzerland. Inorganic agents, such as CrO_3, $CrCl_3$, NaOAc, quartz and oxalic acid, were from MERCK, Darmstadt, Germany, and solvents like CH_3CN, EtOH and acetone, as well as aqueous acids and bases like HCl, H_2SO_4, HOAc and NH_3 from Riedel-de Haën, Frankfurt, Germany. Silica gel type CHROMOSORB W-AWDMC S, 60–80 mesh, was from Lehmann & Voss, Hamburg, Germany.

Isotopically enriched ^{50}Cr ($\approx 95\%$) in metallic form was purchased from EURISO-TOP, Groupe CEA, Saint-Aubin Cedex, France and CHEMOTRADE, Leipzig, Germany. The isotopic composition for both supplies, was: ^{50}Cr $94.7 \pm 0.4\%$, ^{52}Cr 4.84%, ^{53}Cr 0.37%, ^{54}Cr 0.09%. It was confirmed by ICP-MS measurements at the ZCH, Forschungszentrum Jülich, Germany. The chemical impurities (in ppm), as specified by the supplier, were: Ti (< 30), Mn (< 10), Fe (< 250), Ni (< 40), Cu (80), Al (780), Si (200), and Ca (150).

2.2 Radioactive tracers

Radiometric methods were used to quantify the chemical processes. Absolute separation efficiencies were determined using γ-ray spectrometry. The following tracers, partly no-carrier-added (n.c.a.), were used: ^{52}Mn, ^{54}Mn, ^{51}Cr, ^{48}V, ^{59}Fe and ^{86}Rb. The composition of the tracer solutions and their production methods are described in Sect. 3.1.

2.3 Instruments

Exact pH measurements were done using the pH meter CG 838 and the glass electrode type N5900A from SCHOTT, Mainz, Germany. Gravimetric weighings were done using the digital weight AT 261 Delta-Range from METTLER-TOLEDO. Colorimetric determination of concentrations was performed by the UV/VIS spectrophotometer UV 160 A from SHIMADZU, Japan. The fraction collector used was of type RediFrac from AMERSHAM-PHARMACIA, Sweden. Self-constructed columns with inner diameters $\varnothing_i$ for ion chromatography were used with a standard cut on the top allowing a connection of a drop funnel as eluent reservoir with air pressure supply and a glass frit on the bottom followed by a small manual teflon valve and a connection to a teflon tube guiding to the fraction collector in the volume, *i.e.* in the drop mode. The columns were filled by an aqueous suspension of the respective resin adjusting the desired filling level h.

Semi-quantitative radiochromatograms of eluate fractions were registered using the γ-counters Cobra Auto-Gamma and Minaxi Auto-Gamma 5000 from PACKARD. Quantitative γ-ray spectrometry was performed using Ge(Li) and HPGe detectors from CANBERRA and PERKIN ELMER/ORTEC coupled to signal transduction units containing Module Power Supply 4001, Bias Supply 459 or 660 and Amplifier 571, 572 or 672 from PERKIN ELMER/ORTEC. Graphical presentation and peak area analysis of the measured γ-ray spectra were performed using the GammaVision_2.0 software from PERKIN ELMER/ORTEC. The detectors were carefully calibrated concerning energy and efficiency (as a function of energy, sample distance and geometry, cf. [3]) with suitable γ-ray emitting standard sources from PTB, Braunschweig, Germany and AMERSHAM International. All nuclide specific parameters were taken from [28].

3. Experimental

3.1 Preparation of radioactive tracers

3.1.1 Bulk tracer solution (BTS)

The solution was generated by dissolving thick chromium discs ($\sim 400\,mg/cm^2$) of natural isotopic composition irradiated with 20 MeV protons. The nuclides were formed mainly by the following reactions: $^{52}Cr(p,n)^{52}Mn$, $^{54}Cr(p,n)^{54}Mn$ and $^{52}Cr(p,pn)^{51}Cr$. After a 5 h bombardment with a beam of 4 μA, the target was dissolved in hot 7.7 M HCl, separated from insoluble Cr_2O_3 by filtration and evaporated to dryness. The residue was taken up in water and diluted in such a way, that the concentration of chromium trichloride was 96.1 mM. On average, 10 days elapsed until the first use of the BTS; the colour of the solution got converted from dark geen to weakly violet.

3.1.2 N.c.a. $^{52,54}Mn^{II}$

Chemically pure n.c.a. $^{52,54}Mn^{II}$ was produced by alkalisation of the BTS with NaOH aq, subsequent oxidation of Cr^{III} to chromate using H_2O_2 and addition of ferric chloride. The hydroxide precipitate was separated by filtration, dissolved in 7.7 M HCl and the carrier removed using a strong anion-exchange resin column conditioned with 7.7 M HCl. The resulting clear and colourless effluent was evaporated to dryness and the residue dissolved in a small amount of H_2O. The final tracer solution contained pure n.c.a. $^{52,54}MnCl_2$ with a pH of about 4.

3.1.3 $^{51}Cr^{VI}$, $^{51}Cr^{III}$

Radionuclidically pure ^{51}Cr (27.7 d) with some chromium carrier (^{51,nat}Cr) was mainly used as chromate. As educt, alkaline $Na_2[^{51,nat}CrO_4]$, representing the waste in the production process of the n.c.a. $^{52,54}Mn^{II}$ tracer solution, was utilized. The chromate solution was purified from Na^+ and OH^- by passing it through a strong cation-exchange resin column in H^+ form. The resulting effluent was chromic acid, $^{51,nat}CrO_3 \cdot aq$. Solutions of chemically and radionuclidically pure $^{51,nat}CrCl_3$ were derived therefrom by addition of HCl and H_2O_2 at elevated temperature, followed by several evaporations. The final residue was dissolved in H_2O.

3.1.4 N.c.a. $^{48}V^{V}$

Deuteron irradiation of chromium metal generated ^{48}V (16.0 d), mainly by $^{50}Cr(d,\alpha)^{48}V$ reaction. The irradiated target was dissolved in hot 7.7 M HCl, evaporated and re-dissolved in 0.1 M HCl. H_2O_2 was added and the solution allowed to pass through a strong anion-exchange resin in Cl^- form. The n.c.a. peroxovanadate $[^{48}VO(O_2)_2(H_2O)]^-$ [29] fixed on the column was eluted with 7.7 M HCl after washing the column with 0.1 M HCl. The effluent was evaporated and the residue dissolved in H_2O, resulting in pentavalent $^{48}V^V$ aq (several species may exist simultaneously, most probably $[VO_2(H_2O)_4]Cl$ might be present).

3.1.5 $^{86}Rb^I$

^{86}Rb (18.7 d) was chosen as alkali model ion. It was generated by the $^{85}Rb(d,p)^{86}Rb$ reaction, using Rb_2CO_3 of natural isotopic composition as target. After irradiation, the target pellet was dissolved in 7.7 M HCl. The evaporated residue was taken up in H_2O and the concentration adjusted to 117 mM $^{86,nat}Rb$ in the form of its chloride.

3.1.6 $^{59}Fe^{III}$

The ^{59}Fe tracer (44.5 d) was produced by the $^{58}Fe(n,\gamma)$ reaction. For this purpose metallic iron discs of natural isotopic composition were irradiated with thermal neutrons at the research reactor DIDO at Jülich. After bombardement, the metal was dissolved in 7.7 M hot HCl in the presence of H_2O_2. The solution was evaporated and the residue dissolved in 0.1 M HCl, adjusting the concentration to 179 mM $^{59,nat}Fe$ as trichloride.

3.2 Separation system Mn^{II}/Cr^{III}

3.2.1 Cation-exchange chromatography in presence of HCl

Standard glass columns ($\varnothing_i = 10$ mm) filled with DOWEX 50W×8, 50–100 mesh, to $h = 285$ mm were used. The column was conditioned with 150 mL of 7.7 M HCl followed by 100 mL of H_2O. To start with, 1 mL of the BTS was given onto the column. After the initial fixation of the ions in the upper resin layer, the elution was conducted with HCl solutions of defined concentrations.

3.2.2 Cation-exchange chromatography in presence of oxalate

After loading the column ($\varnothing_i = 5$ mm, DOWEX 50W×8, 200–400 mesh, Na^+ form, $h = 120$ mm) with 1 mL of the BTS, elution was performed with a 30 mM oxalic acid solution, containing 100 mM $NaClO_4$ and 10 mM Na_2HPO_4. Furthermore, the eluent had been adjusted to pH 7.3 with about 6 mL of a 10 M NaOH solution.

3.2.3 Anion-exchange chromatography in presence of oxalate

In first experiments the column ($\varnothing_i = 5$ mm, DOWEX 1×8, 100–200 mesh, $h = 135$ mm) was converted to the oxalate form applying the conditioning sequence: 80 mL of 3.3 M HCl, 80 mL of H_2O and 100 mL of 0.2 M disodium oxalate (Na_2ox) solution at pH 7.8. 1 mL of the BTS was pre-complexed with sodium oxalate at > 80 °C for 10 min, adjusting a molar ratio Cr : ox to 1 : 5. The column was loaded by the resulting dark-violet solution, leading to a complete fixation inside the upper resin layer of 20 mm. The elution of n.c.a. radiomanganese(II) was enabled with 0.3 M HCl (retention volume RV = 14.4 mL) and after a RV of 83 mL chromium(III) was desorbed by means of 3.3 M HCl (RV 91 mL) (cf. [30]).

In progressive experiments, the resin in Cl^- form was used (Column: $\varnothing_i = 5$ mm, DOWEX 1×8 resin, 100–200 mesh, $h = 113$ mm). 1 mL of BTS was pre-complexed (Cr : ox = 1 : 5), fixed in the upper resin layer and the n.c.a. radiomanganese was eluted with a 1 mM Na_2ox solution. The final Cr elution was done using 3.3 M HCl. Optimization of pre-column-derivatization (PCD) was achieved by the following method. Inside a small closed vial, the 5-fold molar excess of Na_2ox with respect to chromium of the BTS was dissolved in 1 mL H_2O. 1 mL of the BTS was added immediately before the beginning of the heating. At the start of the reaction ($t = 0$) the vial was introduced in an oil bath of chosen temperature. After the desired reaction time, the vial was quickly removed and transferred to an ice bath to hold the complexation reaction. The reaction mixture was then analyzed by the anion-exchange chromatography. The n.c.a. radiomanganese fraction was eluted with 1 mM Na_2ox within 65 mL followed by the chromium fraction using 3.3 M HCl.

3.2.4 Anion-exchange chromatography in presence of HCl

A temperable column ($\varnothing_i = 5$ mm, DOWEX 1×8, 100–200 mesh, Cl^- form, $h = 175$ mm, conditioned with eluent, defined temperature T^* of the thermostat supplying the heat mantle of the column) was used applying HCl solutions of different concentrations as eluent. The preparation of the separation samples was done by evaporating a mixture of 100 µL BTS and 100 µL $[^{59}Fe]FeCl_3$ tracer solution. The dry residue was dissolved in 1 mL of eluent by heating. The ^{59}Fe tracer was used in test studies to optimize the separation of Fe^{III} carrier from n.c.a. $^*Mn$ (cf. Sect. 3.4). The sample was given onto the column, and the elution started directly after the sample was completely adsorbed into the resin bed. The elution was accelerated with the aid of air pressure, so that the speed was 30 mL/min.

3.3 Separation system Mn^{II}/Cr^{VI}

In order to obtain Mn and Cr in the desired oxidation states (Mn^{II}/Cr^{VI}) the sample solution was prepared by adding 1.2 mL of 1 M NaOH followed by 1 mL of 3 M H_2O_2 (dropwise) at elevated temperature to 1 mL of the BTS in a three-necked flask. After evaporation of the solvent at 180 °C (oil bath) the dry and light-yellow residue was maintained for further 10 min at that temperature to complete the peroxide decomposition. The warm residue was dissolved in 2 mL of H_2O and colloidal $^{52,54}MnO_2$ was reduced by addition of 1 mL glacial acetic acid through the process:

$$HOAc + Cl^- \rightleftharpoons OAc^- + HCl$$

followed by

$$MnO_2 + 4HCl \rightarrow MnCl_2 + Cl_2 + 2H_2O\,.$$

The chloride ions stem from the initial BTS, containing $CrCl_3$. Direct reduction with HCl should be avoided, since in the subsequent evaporation step a reduction of the acid chromate can occur according to:

$$6HCl + CrO_3\,aq \rightarrow CrCl_3 + 1.5Cl_2 + 3H_2O\,.$$

The orange and slightly acetic acid solution (pH $\sim$ 4) was evaporated under mild conditions (oil-bath $\leq 120\,°C$) to dryness.

3.3.1 Solid phase extraction of Cr^{VI}

An extraction column of $\varnothing_i = 10$ mm, filled up to $h = 13$ mm with DOWEX 1×10, 200–400 mesh was used. Prior to the separation, the resin was converted to the perchlorate form by rinsing it with 100 mL of 1 M $NaClO_4$ until the effluent showed no reaction with Ag^+ ions. This was done to avoid reduction of the acid chromate by chloride ions. The evaporated red-orange residue was dissolved in 2 mL H_2O. White $SiO_2 \cdot xH_2O$ stemming from the flask wall got precipitated and was filtered off *via* glass wool. The slightly acidic Mn^{II}/Cr^{VI} solution (pH $\sim$ 5.3) was transferred to the extraction column. The elution of radiomanganese proceeded with pure water (pH $\sim$ 6.5). Most of the fixed (isotopically enriched) chromium could be reductively desorbed as Cr^{III} by means of a solution containing 1 M H_2SO_4 and 0.1 M Na_2SO_3.

3.3.2 Liquid–liquid extraction of Mn^{II}

The experimental extraction efficiency of each step of the extraction procedure was quantified *via* γ-ray spectrometry by analyzing an aliquot of each fraction. The procedure started with the dissolution of the evaporated red-orange residue (Mn^{II}/Cr^{VI}) in 5 mL of a special aqueous phase (SAP) which was transferred into an extraction funnel. The pH of the final solution was about 9.8.

The SAP represents an ammonia solution, saturated with Hacac, which is freshly prepared by shaking 3 times 20 mL of 1 M NH_3 with 10 mL of 0.5 M Hacac in $CHCl_3$. After each shaking, the organic phase was discarded. The final SAP remained somewhat turbid and had pH 10.4. Generally, one minute for each extraction was sufficient. For the determination of the nuclide distribution, aliquots were taken from each separated phase and analysed by γ-ray spectrometry.

In the first and most important extraction step, 5 mL of the extracting solution ES (0.5 M Hacac in $CHCl_3$) were added to 5 mL of SAP containing the radionuclides. After the first extraction, the organic phase was transferred to a second funnel and the aqueous one extracted with further 5 mL of fresh ES. The remaining aqueous phase, containing the chromate, was collected in the case of isotopically enriched chromium for recovery. The united organic phases were washed by shaking with the same volume of SAP to remove physically co-extracted chromate. For back-extraction, the organic phase was treated with an equal volume of 1 M HCl. The organic phase was discarded. For removal of organic traces the aqueous phase was passed through a reversed phase cartridge and evaporated. The residue, containing the desired n.c.a. radiomanganese, was taken up in an aqueous medium.

3.4 Separation system $Mn^{IV}/Cr^{VI}/Fe^{III}$

Thin targets, containing about 5 mg of metallic chromium, were dissolved in 2 mL of hot 3 M HCl. In test runs the procedure was started with 1 mL of the BTS. Then a magnetic stirrer, 1 mL of water and 1 mL of 10 M NaOH were added. Further addition of about 1 mL of a 10 M H_2O_2 solution oxidized the chromium(III) under heating to light yellow chromate. Thereafter, 1 mL of a 6 mM $FeCl_3$ solution was added dropwise, whilst the peroxide decomposed catalytically and the Fe^{III} got precipitated as flaky-brown hydroxide. N.c.a. $^*MnO_2 \cdot nH_2O$ was co-precipitated with the non-isotopic carrier. After short boiling ($\sim$ 1 min) the solution was pressed through a special filter column by means of a slight air pressure. The filter column ($\varnothing_i = 10$ mm) consisted of a lower silica gel layer (60–80 mesh) and an upper layer of coarse-grained quartz powder (200–800 μm), which adsorbed most of the voluminous ferric hydroxide. Each layer was about 1 cm thick. The filter columns were conditioned before use by 5×2 mL of 7 M HCl, 5×2 mL of H_2O, and 2×2 mL of 0.1 M NaOH. The ferric hydroxide precipitate was washed 8 times with 1 mL of warm 0.1 M NaOH and the chromate filtrate collected for recovery purposes. Iron and the co-adsorbed radiomanganese were desorbed from the column by means of 8 portions of 1 mL warm 6 M HCl.

The collected Mn-fraction was separated from the Fe^{III} carrier by solid phase extraction using the heated strong anion-exchange column DOWEX 1×8, 100–200 mesh, Cl^- form, $\varnothing_i = 5$ mm, $h = 175$ mm, $T^* = 75\,°C$, applied in the anion-exchange chromatography in the presence of HCl (cf. Section 3.2.4). If no additional separation of Cr^{III} traces was desired, the column was conditioned with 5 M HCl. In test runs, the Fe^{III} separation was quantified using the radiotracer ^{59}Fe or by photometric measurement of $[FeCl_4]^-$ in 11.5 M HCl at $\lambda = 363$ nm. The $^*Mn^{II}/Fe^{III}$ solution was pressed through the column, applying slight air pressure. The filtrate was evaporated to dryness and re-dissolved in an aqueous medium. It contained pure n.c.a. radiomanganese(II).

3.5 Chromatograms and elution profile

Most of the qualitative chromatograms and elution profiles shown in this work have a curve shape, resulting from γ-ray counting of the eluted column fractions. The γ-ray energy windows 660–1000 keV and 200–360 keV were chosen for counting $^{52,54}Mn$ and ^{51}Cr, respectively. The correct and absolute nuclide fraction inside each "peak big fraction" was obtained by unification of the differential fractions (*i.e.* of all elution fractions contributing to a peak) to a total of 2 or 3 large fractions. These fractions were diluted to equal volumes (geometries) and measured γ-spectrometrically.

3.6 Targetry

For production of ^{51}Mn the target was prepared in two steps, namely conversion of target material to $^{50}CrCl_3$ and preparation of an $Al_4\cdot{}^{50}CrCl_3$ sandwich. These two steps are described below.

3.6.1 Preparation of $^{50}CrCl_3$

The process was similar to the first part of the preparation of $^{50}CrO_3$ for electrodeposition purposes (cf. Fig. 1) [31]. The production cycle started with one of the two available chemical forms of ^{50}Cr, the metal or the sesquioxide (for details cf. [32]). The metal was dissolved in hot 5 M HCl, evaporated to dryness and dried at a temperature > 180 °C for 30 min under a flow of dry air. In contrast, the sesquioxide was initially fused in a hot oxidizing salt melt of $NaNO_3$ and K_2CO_3, and the cooled melt cake dissolved in 5 M HCl. The nitrate present was removed by several evaporation cycles with 8 M HCl or by passing the solution through a cartridge of suitable dimension, containing strong anion-exchange resin in Cl^- form, followed by evaporation. The nitrate-free, dry residue was dissolved in 3 M HCl, and Cr^{VI} reduced to Cr^{III} by addition of H_2O_2. The solution was evaporated and dissolved again in 3 M HCl several times to ensure complete peroxide removal. The final residue was dissolved in hot water and 0.5 M NH_3 was added to precipitate chromium as $^{50}Cr(OH)_3$. The precipitate was centrifuged off and the clear solution containing alkali ions was discarded. After two further washing steps with 1 mM NaOH, the $^{50}Cr(OH)_3$ was processed like the pure metal. Before preparing the $Al_4\cdot{}^{50}CrCl_3$ pellets, $^{50}CrCl_3$ was further dried under heat and vacuum for several hours.

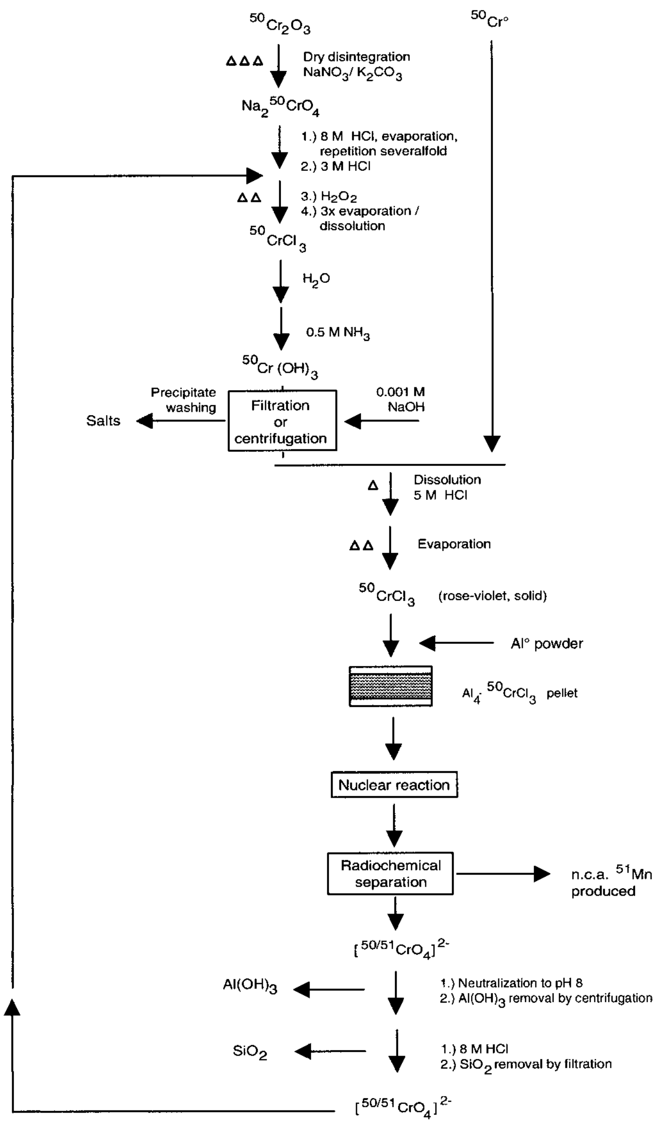

Fig. 1. Flow sheet for the production and reprocessing of $Al_4\cdot{}^{50}CrCl_3$ targets.

3.6.2 Preparation of $Al_4\cdot{}^{50}CrCl_3$ sandwich

The $Al_4\cdot{}^{50}CrCl_3$ pellet was made by pressing a mixture of 70 mg $^{50}CrCl_3$ and 50 mg Al° powder between two polyethylene (PE) foils in a pellet press ($\varnothing_i = 13$ mm) at 10 t/cm^2 (10^3 bar) for 10 min. The pellet thus contained 23 mg (0.46 mmol) of chromium-50. The resulting pellet (cf. Fig. 2) had a thickness of about 1 mm, was mechanically stable, but very hygroscopic, since the present electron donor Al° electrochemically catalyses a water-complexation of chromium (cf. [29]). The moisture uptake was diminished by Al° cover foils (≥ 10 µm, *e.g.* 25 µm, cf. Fig. 2), which were pressed together with the powder mixture. In spite of this improvement, the pellet had to be transfered directly to a desiccator after removal from the press until its use, where it remained under vacuum.

3.7 Irradiations for production of ^{51}Mn

The $Al_4\cdot{}^{50}CrCl_3$ sandwich was placed in a 2π water-cooled target holder and irradiated with 13.4 MeV deuterons. In cases of two additionally placed 30 µm Al° foils in front to prevent potential losses of target material during the irradiation, the deuteron energy incident on the matrix pellet was 12.8 MeV. The target system is similar to the one used by Denzler *et al.* [11]. Irradiation tests showed that for focussed beams the upper flux limit was already reached at 2 µA. In contrast, the pellets remained stable up to 3.5 µA, if the beam was wobbled to a plane of about 1 cm^2. After irradiation, the pellet was dissolved and ^{51}Mn was radiochemically separated as described in Sect. 3.4.

In one irradiation experiment a beam current of 3 µA was applied for 1 h. The irradiated sandwiched pellet was dissolved in HCl. Two aliquots were taken. One was processed

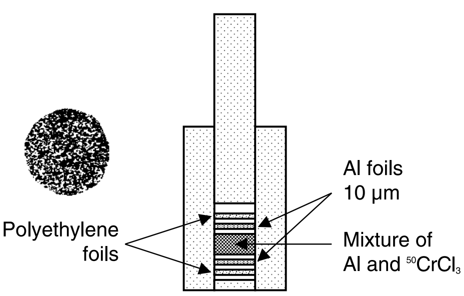

Fig. 2. Left hand: Check of the $Al_4\cdot{}^{50}CrCl_3$ pellet without covering Al foils. Light areas = Al°, dark areas = $^{50}CrCl_3$. Right hand: Arrangement of $Al_4\cdot{}^{50}CrCl_3$ and foils inside the pressing tool.

using the co-precipitation procedure and the other was used as such to quantify the chemical losses during the workup process. Both the resulting fractions, containing Mn and Cr, respectively, were measured γ-spectrometrically several times over a long decay period to enable a multidecay analysis. The latter analysis was absolutely necessary to quantify the almost pure positron emitter ^{51}Mn *via* an assay of the annihilation γ-peak (cf. [3]).

3.8 Recovery of ^{50}Cr

After radiochemical separation of ^{51}Mn *via* the precipitation process (cf. Sect. 3.4), the remaining enriched target material in the Cr-fraction existed as [^{50}Cr]chromate, as shown in the flow sheet, Fig. 1. After decay of the short-lived radionuclides this fraction was neutralized to pH 8 with 2 M HCl. The $Al(OH)_3$ precipitate was centrifuged off. The clear, yellow solution was further acidified with 8 M HCl and stirred for 30 min at 80 °C. The $SiO_2 \cdot xH_2O$ precipitate was filtered off and H_2O_2 added to the warm and clear orange filtrate. $^{50}CrCl_3$ was formed *via* blue $^{50}CrO_5$ and the process cycle was closed. The preparation of a new target was done as described above starting at the point after the desintegration of the chromium sesquioxide.

4. Results and discussion

Prior to the high current irradiations and production of ^{51}Mn, some basic investigations were performed to develop the best suited separation method for n.c.a. ^{51}Mn from the target matrix. All techniques are compared and the optimum procedure is described.

4.1 Separation system Mn^{II}/Cr^{III}

4.1.1 Cation-exchange chromatography in presence of HCl

An easy access to the Mn/Cr separation problem seemed to be the simple cation-exchange chromatography, since after dissolution of the irradiated metallic chromium in HCl manganese and chromium are present in different oxidation states (Mn^{II}, Cr^{III}). In principle a separation applying cation-exchange chromatography seemed to be realizable while using an "old" bulk tracer solution (BTS, cf. Fig. 3), However, the elution volume of the Mn-fraction was large, even with such small amounts of chromium carrier as 5 mg (0.1 mmol). This problem would be worse in the case of real target samples weighing about 100 mg (2 mmol) chromium. A second problem arose due to non-removable fixation of a fraction of Cr^{III} in the upper resin bed, possibly due to coordinative bonds of the resin sulfonyl groups with the trivalent species. The major problem occurred, when a "freshly" prepared BTS was tested in the same manner. As seen in Fig. 3, chromium was eluted in three fractions, one of them exactly together with Mn^{II} (cf. [33]). This behaviour is explainable by the hydration isomerism of Cr^{III}, as a result of kinetic inhibition of ligand exchange (Cl^- *vs*. H_2O) in the octahedric coordination shell. Thus different isomers with different effective complex charges exist simultaneously, depending on the pH and ligand concentration [29, 34–36]. Unfortunately

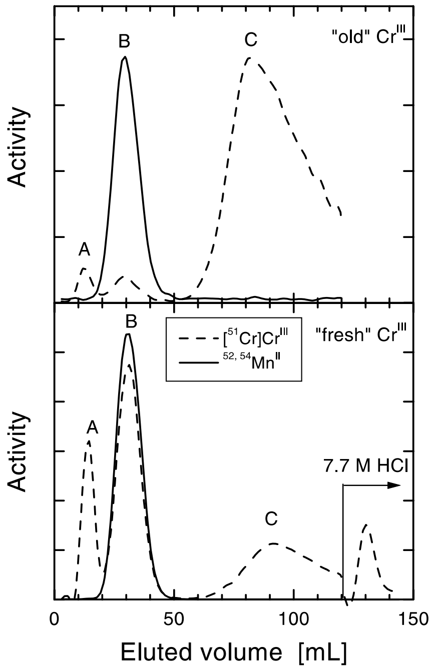

Fig. 3. Top: Radiochromatogram of an "old" (> 10 d) bulk tracer solution (BTS), bottom: Radiochromatogram of a "fresh" (< 2 d) BTS; both obtained using a γ-counter. Column: DOWEX 50W×8, 200–400 mesh, Na^+ form, $\varnothing_i = 5$ mm, $h = 125$ mm. Eluent: 1 M HCl. Elution speed: 2.3 ± 0.5 mL/min. A ≡ $[CrCl_2(H_2O)_4]Cl \cdot 2H_2O$ (dark-green), B ≡ $[CrCl(H_2O)_5]Cl_2 \cdot 1H_2O$ (light-green), C ≡ $[Cr(H_2O)_6]Cl_3 \cdot$ (violet).

$[CrCl(H_2O)_5]^{2+}$ is always eluted together with the desired $^*Mn^{II}$, especially in fresh $^*CrCl_3$ solutions obtained after dissolving the target.

4.1.2 Cation-exchange chromatography in presence of oxalate

An improvement in the Mn/Cr separation was expected by addition of a stronger complexing agent to the system than chloride. Since Cr^{III} has a stronger tendency for complex formation (cf. *e.g.* [37]) compared to Mn^{II}, Cr^{III} should be eluted prior to Mn^{II}, using a cation-exchange resin as static and dissolved complexing agents as mobile phase. Thus, the elution sequence would be completely reversed. Oxalate was chosen as the complexing agent, since the corresponding acid is easily removable *via* oxidation [38] after the chromatographic separation of n.c.a. radiomanganese(II). In view of the necessary optimum concentration of oxalate in the eluent, the relative molar fractions α_i of the different metal oxalate complex species i (i = M, ML, ML_2, ...) were calculated in dependence of the free complex ligand concentration [32] using documented stability constants [37, 39]. The resulting function plot is shown in Fig. 4. In order to guarantee all free oxalate molecules to be non-protonated, a pH of 7 or higher is obligatory (cf. $pka_1 = 1.23$, $pka_2 = 4.17$ [40]). According to Fig. 4 a chromatographic separation may be enabled by applying a free oxalate concentration of 0.1 mM, where Cr^{III} exists nearly completely in the form of anionic complex species, whilst manganese would remain fixed on the strong cation-exchange resin as bivalent cation. In practical chromatographic separations, however, oxalate concentrations as high

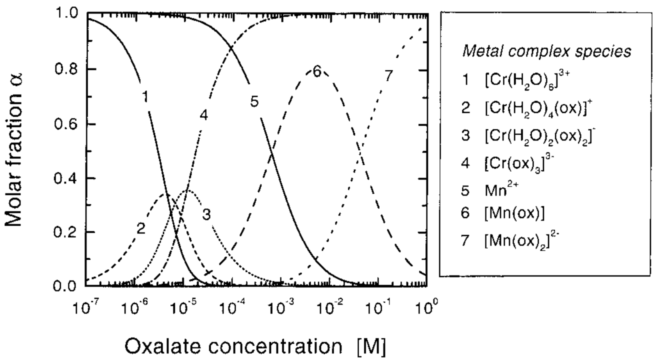

Fig. 4. Molar fraction α of the (metal chelate) species in the system metal ion/oxalate/H_2O as a function of free chelator (oxalate) concentration. The complex stability constants used are: p$K_1 = 5.34$, p$K_2 = 5.17$, p$K_3 = 4.93$ for Cr^{III} [39] and p$K_1 = 3.2$, p$K_2 = 1.4$ for Mn^{II} [37].

as 30 mM were necessary, resulting in an unexpected elution sequence of the two elements similar to the one found in the cation-exchange chromatography in the presence of HCl. The reason again is the kinetic inhibition of complex formation even with the stronger ligand oxalate compared to chloride. The resulting contamination of the Mn-fraction with about 3% of the target chromium was unacceptable.

In extension, a pre-column derivatization (PCD), *i.e.* a pre-complexation of the sample cations, was conducted with sodium oxalate by heating at $> 80\,°C$ for 2 min prior to the chromatographic separation. This resulted in the expected elution sequence: Cr before Mn. The chromium contamination in the Mn-fraction could be reduced to less than 0.1% of the initial chromium, depending on the Cr : oxalate ratio during the primary complexation. However, increasing purity of the radiomanganese is coupled with a decreasing radiochemical yield. At a molar Cr : oxalate ratio of 1 : 2 the *Mn yield is 75% and at 1 : 3 the yield is only 23%. The manganese lost is co-eluted with chromium.

4.1.3 Anion-exchange chromatography in presence of oxalate

Since the cation-exchange chromatography did not give a satisfactory separation of chromium from manganese, the elution sequence was reversed applying anion-exchange chromatography after PCD with oxalate. The distribution coefficients of the two metal ions Mn^{II} and Cr^{III} in oxalate solution have already been determined [41]. Analogous separation systems using malonate or tartrate as complexing agents have also been investigated [42, 43].

In first experiments, the column resin DOWEX 1×8 was converted from the chloride to the oxalate form. By this way, the manganese was almost quantitatively eluted within the first 40 mL of the dilute HCl eluent, with a radiochemical yield of 99.5%. However, the chromium contamination of 1.5% in the Mn-fraction was too high. Thus, this separation mode is more suitable to obtain Cr-fractions free of Mn rather than Mn-fractions free of Cr. Subsequently the resin conditions were changed to maintain it in the chloride form and a 1 mM disodium oxalate solution served as eluent. Manganese was eluted first. Thereafter, chromium was eluted by using 3.3 M HCl. PCD was optimized regarding reaction time and temperature while applying this separation system. Thus for a molar Cr : oxalate ratio of 1 : 5 reacting for 10 min at 100 °C, as low as 0.015% of the total chromium was eluted with the manganese fraction. However, the radiochemical yield of manganese had a maximum of about 89%. Further efforts were devoted to optimize the Mn/Cr separation by conditioning the anion-exchange resin with a defined anion ratio of chloride to oxalate. Again, as eluent dilute oxalate solutions were used. However, the quality of separation deteriorated with the rising resin conditioning ratio of oxalate to chloride. This behaviour prohibits a resin conditioning with any amount of oxalate.

4.1.4 Anion-exchange chromatography in presence of HCl

The separation is based on the formation of chloro complexes [44, 45], which is interestingly more strongly marked for Mn^{II} than for Cr^{III} [37]. The complexing equilibrium strongly depends on the temperature; the separation of Mn from Cr thus being strongly improved with increasing separation temperature. This method was investigated at macroscopic level [33] and has also been applied to separate n.c.a. ^{51}Mn from irradiated ^{50}Cr [22]. We optimized the separation conditions using DOWEX 1×8, finding best results for the given column dimension at column temperatures of $\geq 80\,°C$, applying ≥ 11 M HCl as eluent. An additional advantage of this procedure is the simultaneous separation of a probable Fe^{III} impurity, as shown in Fig. 5. However, as in all chromatographic separations, the elution volume of the manganese fraction becomes high, when the column dimensions are adapted to higher amounts of target chromium.

4.2 Separation system Mn^{II}/Cr^{VI}

The basis of these separations was the oxidative transformation of Cr^{III} to anionic Cr^{VI} using H_2O_2 in alkaline medium followed by selective reduction of Mn^{IV} to Mn^{II} in acidic medium. Thus an efficient separation of Mn^{II} cations from Cr^{VI} anions is enabled.

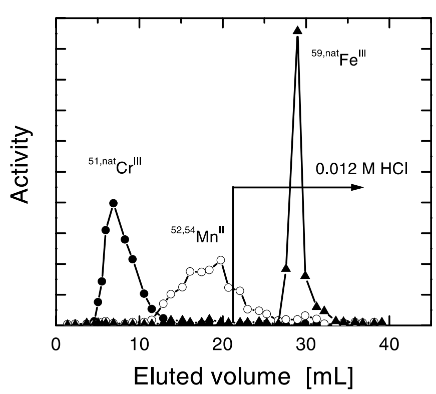

Fig. 5. Anion exchange chromatographic purification of the metal cations: n.c.a. $^{52,54}Mn^{II}$, $^{51,nat}Cr^{III}$ and $^{59,nat}Fe^{III}$. Separated amounts: 10 μmol Cr and 18 μmol Fe. Column: DOWEX 1×8, 100–200 mesh, Cl^- form, $\varnothing_i = 5$ mm, $h = 175$ mm. Thermostat temperature $T^* = 75\,°C$, effective column temperature about 70 °C. Primary eluent for Cr^{II}/Mn^{II} separation: 11.5 M HCl, secondary one after 21 mL: 0.012 M HCl for Fe^{III} elution.

4.2.1 Solid phase extraction of Cr^{VI}

The method [46] is based on selective fixation of chromate on solid phase columns of strong anion-exchange resins in perchlorate form. The procedure has been applied to separations of n.c.a. ^{51}Mn from ^{50}Cr metal targets [26, 27]. In our studies, the divalent n.c.a. radiomanganese was found almost quantitatively inside the aqueous filtrate. However, it was contaminated with about 3% chromium, which was unaccepatably high. The origin of this contamination lies in the oxidation of the organic resin in the presence of slightly acidic chromate [47, 48] leading to Cr^{III}, which is washed out together with Mn^{II}. The situation deteriorated while using the same resin in chloride instead of perchlorate form. In this case, about 20% of the total chromium was found in the Mn^{II} filtrate.

4.2.2 Liquid–liquid extraction of Mn^{II}

In trace analysis, liquid–liquid extraction has been applied to concentrate Mn^{II} [49, 50]. The desired n.c.a. radiomanganese is selectively extracted into the added organic phase, from which it is back-extracted in the final step. We determined the extraction curve for Mn^{II} using Hacac in $CHCl_3$ as extracting agent. The resulting experimental extraction curve for our extraction system is shown in Fig. 6; it is distinctly different from the curve reported in the literature [50]. The difference results possibly from our non-ideal conditions where macroscopic amounts of slightly acidic chromate and acetate contribute to the aqueous solution containing n.c.a. $^*Mn^{II}$. Thus, the present extraction curve is not generally valid but only for the extraction conditions in our experimental work, which would be of relevance to the production of ^{51}Mn. Our curve shows a quantitative Mn^{II} extraction above pH 8. Sufficient extraction, however, already occurs at pH 7, although the molar fraction of the deprotonated $acac^-$ is still very low.

The separation experiments revealed that the Mn^{II} extraction already in the first step is selective and almost quantitative (only 0.02% Cr but 98% Mn in the organic phase). In the second extraction, a further 70% of the remaining manganese (2% of total manganese) is extracted, but simultaneously some Cr (0.08%) is co-extracted. Thus

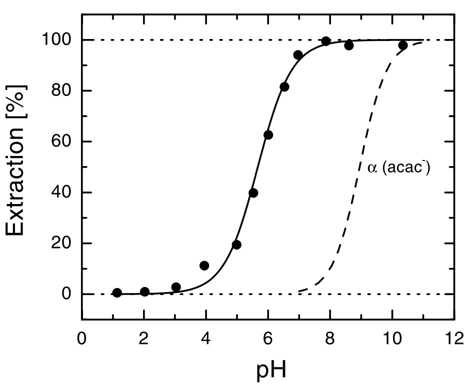

Fig. 6. Extraction of n.c.a. $^*Mn^{II}$ from a 5 mL chromate solution in presence of acetate, plotted as a function of pH. Organic extraction phase contains 5 mL 0.5 M Hacac in $CHCl_3$. Additionaly shown is the mole fraction (α [%]) curve for the anion $acac^-$, stemming from proton dissociation of Hacac in alkaline media: $pK_S = 8.95$ [60].

the second extraction step is not very efficient and should be omitted. Due to the washing in the third step, about 75% of the co-extracted chromium can be transfered back from the organic Mn-fraction to the aqueous phase. In the final extraction step, n.c.a. radiomanganese (99.92%) and most of the contaminating chromium traces (85%) are back-extracted into the acid aqueous phase. It contains 98.5% of initial manganese and 0.005% of initial chromium.

4.3 Separation system $Mn^{IV}/Cr^{VI}/Fe^{III}$

In this method the initial Mn^{II}/Cr^{III} species are oxidized to Mn^{IV}/Cr^{VI} in alkaline medium and the n.c.a. radiocolloid $^*MnO_2 \cdot xH_2O$ is co-precipitated with some added non-isotopic Fe^{III} carrier. The precipitate is separated from the chromate solution and finally the Fe carrier is selectively removed, resulting in a pure n.c.a. radiomanganese fraction. The radiochemical separation efficiency was confirmed in four runs. The chromium content in the Mn/Fe-fraction was $0.13 \pm 0.10\%$ (of total chromium) and the radiochemical separation yield of Mn was $99.7 \pm 0.2\%$. Optimum efficiency data were 0.03% Cr and 99.95% Mn in the Mn/Fe-fraction. The separation efficiency was almost independent of the amount of added carrier, whenever the precipitation temperature was sufficiently high [51]. Thus, a quantitative precipitation is also possible with Fe amounts as low as 0.5 mg (9 μmol), which makes the filtration and the subsequent removal of Fe rather easy.

For removal of the Fe carrier two methods have been applied. In the first one, Fe^{III} is extracted by liquid–liquid extraction using diethylether [52–54] or diisopropylether [55–57]. The second one makes use of solid phase extraction of an anionic chloro complex, formed in strong hydrochloric acid medium, using anion-exchange resins [6, 13, 15]. Especially the latter technique seemed suited to eliminate Fe^{III}, both selectively and quantitatively, from the n.c.a. radiomanganese fraction [6]. The distribution coefficient D of Fe^{III} at such resins initially increases with increasing HCl concentration and then decreases at high concentrations due to competing chloride ions [14]. The D_{max} at 10 M HCl is $10^{+4.5}$. In order to determine the minimum HCl concentration for a sufficient solid phase extraction of Fe^{III}, systematic studies were conducted, analogous to those on the Mn^{II}/Cr^{III} anion-exchange separations at elevated temperatures (see Sects. 3.2.4. and 4.1.4. above) [32]. It was found that quantitative removal of Fe^{III} is possible at HCl concentrations higher than 2 M; lower concentrations should be avoided.

4.4 Comparison of separation methods

A summary of the techniques used to separate n.c.a. $^*Mn$ from bulk of Cr is given in Table 1. The separation times are estimates for manual processing with uncertainties of ±25%. Thus it may be possible to reduce the required time considerably in an automated process.The most time consuming operation in each process is the evaporation step.

Generally, chromatographic methods are not well-suited when large molar amounts are to be separated, as in the case

Table 1. Summary of radiochemical methods investigated for the separation of radiomanganese from bulk target chromium.

Classification	**Primary treatment**	**Separation method**	**Efficiency** Cr in Mn-fraction/*Mn in Mn-fraction [%]	**Time of separation** [min]	**Dependent on target amount**	**Comment**
Mn^{II}/Cr^{III}	dissolution	CXC with HCl eluent	30/99	50	yes	too much Cr^{III}-complex species
		CXC with oxalate eluent	0.1/75	50	yes	pre-column-derivatization mandatory
		AXC with oxalate eluent	0.02/82	50	yes	pre-column-derivatization mandatory
		AXC with HCl eluent	0.5/95	40	yes	high separation temperature necessary
Mn^{II}/Cr^{VI}	dissolution, oxidation, selective reduction	SPE with AXR	3/99	60	yes	resin oxidation: Cr^{III} in Mn-fraction
		LLE	0.02/98	60	no	reasonable
$Mn^{IV}/Cr^{VI}/Fe^{III}$	dissolution, oxidation, precipitation	co-precipitation with non-isotopic carrier, followed by SPE with AXR	0.03/99	50	no	simple, reproducible

Abbreviations: AXC = anion exchange chromatography, CXC = cation exchange chromatography, AXR = anion exchange resin, LLE = liquid–liquid extraction, SPE = solid phase extraction.

of Mn^{II}/Cr^{III}, where large amounts of target chromium are present in production runs. Apart from this disadvantage, additional problems arise from the inhibited complex kinetics of Cr^{III}. Thus, simple cation-exchange separation (Mn^{II}/Cr^{III}) is impossible, since differently charged water-anion-complexes of Cr^{III} exist simultaneously. This well-known phenomenon, called hydration isomerism, leads to undesired co-elution of one of the complex isomers with effective charge 2+ together with Mn^{II}. Only with the aid of chelators like oxalate, manganese can be separated from chromium (with remaining Cr contamination of $< 0.02\%$) applying anion-exchange chromatography. However, the radiochemical yield (RCY) of *Mn amounting to about 85% (maximum) is low and a pre-column complexation of the sample is mandatory. Chromatographic methods are thus not suitable for separating bulk of Cr from radiomanganese.

The method involving solid phase extraction of slightly acidic chromate is also not very suitable, although it was applied earlier to produce ^{51}Mn [26, 27]. The cause is the resin oxidation by acidic chromate, leading to co-elution of Cr^{III} in the $^{*}Mn^{II}$ filtrate. Alternatively, non oxidisable inorganic anion-exchangers [58, 59] might be applied to extract slightly acidic chromate. However, one has to consider the lower exchange capacity of such exchangers, compared to the polymer based ones; this demands larger column dimensions.

The liquid–liquid extraction method is well suited for a quantitative separation of chromium from radiomanganese in a ^{51}Mn production process. Since vanadium (as vanadate) behaves similar to chromium under the existing conditions, the radiovanadium present (*e.g.* ^{48}V) will be separated together with chromate. The advantage compared to the solid phase extraction, besides the achievable radionuclidic purity of 99.98% and the high RCY of $> 99\%$, is the independence from the amount of target chromium present and the small volume of the final $^{*}Mn^{II}$ solution which needs to be evaporated. Unfortunately, both the extraction methods need a careful and relatively long-lasting treatment of the primary target solution until chromium is quantitatively converted to chromate and manganese is selectively reduced to the bivalent cation.

The co-precipitation method is most suitable to separate bulk Cr almost quantitatively from n.c.a. *Mn, since it is nearly independent of the Cr amounts present (Cr can be separated to an extent of $> 99.9\%$). Other advantages are the high RCY of Mn separation ($> 99.9\%$), simplicity, reproducibility and speed. The speed is only limited by the evaporation step at the end of the separation, where about 10 mL of the hydrochloric aqueous medium have to be removed. Furthermore, other elements and radionuclides present, like ^{48}V (as VO_4^-), Al (as $Al(OH)_4^-$, Al is an additive in $Al_4 \cdot CrCl_3$ targets) or ^{38}Cl (as Cl^-, in case of $Al_4 \cdot CrCl_3$ targets), are separated together with Cr. Since the separated chromium is present as chromate, an easy recovery is enabled in the case of isotopically enriched target chromium, *e.g.* ^{50}Cr. The co-precipitation method also appears to be well-suited for remote or automated processsing [32].

4.5 Choice of the chemical form of the target

In view of the expected maximum production yield of ^{51}Mn, metallic ^{50}Cr° would be the optimum chemical form of the target. However, despite its high melting point of 1903 °C [29] the pure metal is not suitable, since its surface is easily passivated to sesquioxide, which is insoluble in mineral acids. A fast wet-chemical processing of the target after EOB is thus prevented. So far mostly the sequioxide $^{50}Cr_2O_3$ has been applied for production purposes [22–27], since it is chemically stable (m.p. 2275 °C [29]). However, a cumbersome and lengthy dry-chemical digestion in salty oxidation melts ($K_2CO_3/NaNO_3$ or $NaOH/Na^2O_2$) is essential to decompose the sesquioxide. Furthermore, the target preparation is hampered by the hard corundum crystal structure [29], rendering pressing of stable pellets difficult. The trivalent halogenides $^{50}CrX_3$ appear to be good alternatives to the sesquioxide, since they can be processed wet-chemically. The iodide is less suited, since it is easily decomposed at high temperatures. The bromide is thermally more stable than the iodide but is still not suitable. The light halogenides $^{50}CrCl_3$ and $^{50}CrF_3$ are both potentially useful but some expected complications due to HF release during the target workup in the latter case led the choice to $^{50}CrCl_3$ as target material.

Chromium trichloride was chosen as the target, since it can be easily produced and quickly dissolved after irradiation. Although the pure rose-violet compound (without crystal water) is insoluble in water [29], the compound generated by withdrawal of water *via* vacuum drying is not completely water-free and can thus quickly be redissolved. However, due to its layer crystal structure [29] it cannot be pressed to compact and stable pellets. Therefore, aluminium powder was added to stabilize the matrix material, resulting in an $Al_4 \cdot CrCl_3$ target composition. The light metal Al has a cubic dense structure [29], generates only short-lived activation products as ^{24}Na, and improves the target cooling due to its thermal conductivity. On the other hand it has a low melting point (660 °C [29]), reduces the relative ^{50}Cr content of the target (which leads to a reduced ^{51}Mn yield) and might induce the exothermic reaction $^{50}CrCl_3 + Al° \rightarrow {}^{50}Cr° + AlCl_3$, which may cause problems, especially due to the additional heat release.

4.6 ^{51}Mn production using $Al_4{\cdot}CrCl_3$ targets

Production tests were conducted with a 2π water-cooled target holder of copper [11] and 20 mg (0.4 mmol) of 95% enriched ^{50}Cr in the form of $Al_4 \cdot CrCl_3$ pellets. The resulting experimental yields, normalized to 1 μA h, are listed in Table 2. Thus at 3 μA for 1 h, 106 ± 10 MBq of ^{51}Mn were produced at the end of bombardment (EOB). The major radionuclidic impurity in the separated ^{51}Mn-fraction was the short-lived positron emitter ^{52m}Mn ($t_{1/2} = 21$ min) amounting to about 6 MBq at EOB. However, due to its shorter half-life its contribution was significantly reduced at the end of the chemical synthesis (EOS), following the nuclide separation. The radiochemical separation scheme $Mn^{IV}/Cr^{VI}/Fe^{III}$ delivered the desired ^{51}Mn in high radiochemical purity, containing $< 0.1\%$ of the initially present nuclides ^{51}Cr, ^{48}V, ^{38}Cl and ^{24}Na. This means, that the removal of target chromium is done with the same efficiency ($\geq 99\%$). The short-lived ^{38}Cl is the major matrix activity at EOB (61 MBq). No significant loss of the desired radionuclide (^{51}Mn) and of the expensive isotopically enriched ^{50}Cr during the separation process occurred, as was revealed by a comparison with an unseparated aliquot.

Table 2. Experimental thick target yields (Y) for the target system $Al_4 \cdot {}^{50}CrCl_3$ with a total ^{50}Cr mass of 20 mg in the effective energy range $E_d = 12.8 \rightarrow 7.9$ MeV.

Radionuclide	Half-life	Experimental thick target yield	
		[MBq/μA h]	[mCi/μA h]
Mn-fraction			
^{51}Mn	46.2 min	35.516	0.9599
^{52m}Mn	21.1 min	2.079	0.0562
^{52}Mn	5.6 d	0.019	0.0005
Cr-fraction			
^{38}Cl	37.2 min	20.332	0.5495
^{24}Na	15.0 h	2.734	0.07394
^{48}V	16.0 d	0.074	0.0020
^{51}Cr	27.7 d	0.263	0.0071

5. Conclusion

In contrast to the isotopically enriched sesquioxide target ($^{50}Cr_2O_3$), which has been previously used by other workers, an approach has been developed to produce ^{51}Mn *via* targets, which do not have a dissolution problem during the chemical procedure after EOB. With the suggested $Al_4 \cdot {}^{50}CrCl_3$ sandwich a medium scale production of ^{51}Mn has been achieved. The target withstands a 3 μA wobbled beam of 14 MeV deuterons. The thick target yield of ^{51}Mn from the ^{50}Cr(d, n) process over the in-target effective energy range of $E_d = 12.8 \rightarrow 7.9$ MeV amounted to 35.5 MBq/μA h. Simultaneously, the shorter-lived radioisotope ^{52m}Mn was formed; its yield was only 2.1 MBq/μA h. The high matrix activity due to ^{38}Cl (20.3 MBq/μA h) could be chemically separated. For an automated separation process the co-precipitation of Mn^{IV} with added Fe^{III} appears to be best suited regarding separation efficiency, speed, reproducibility, and remote handling. Due to the shorter half-life of ^{52m}Mn, the radionuclidic purity of ^{51}Mn increased to 98%, if 60 min for separation and labelling were considered. In order to achieve higher ^{51}Mn yields, high current targetry needs to be developed, taking into account the subsequent rapid radiochemical separation of radiomanganese.

Acknowledgments. The present work is part of the Ph.D. dissertation of A. T. J. Klein (cf. Report Jül-3553) who thanks the Research Centre Jülich for financial support. The authors are grateful to the operators of the compact cyclotron CV 28 for performing a large number of irradiations, and to the Zentralabteilung für Chemische Analyse (ZCH) for ICP-MS measurements on the isotopically enriched isotopes.

References

1. Schwiegk, H., Turba, F. (Eds.): *Künstliche Radioaktive Isotope in Physiologie, Diagnostik und Therapie*. Vol. 1 and 2, Springer, Berlin, Germany (1961).
2. Wagner, K.: Kernenergie **5**, 853 (1962).

3. Klein, A. T. J., Rösch, F., Qaim, S. M.: Radiochim. Acta. **88**, 253 (2000).
4. West, Jr., H. I., Lanier, R. G., Mustafa, M. G.: Phys. Rev. C **35**, 2067 (1987).
5. Zaman, M. R., Qaim, S. M.: Radiochim. Acta **75**, 59 (1996).
6. Fessler, A., Alfassi, Z. B., Qaim, S. M.: Radiochim. Acta **65**, 207 (1994).
7. Wiegers, C. B., Welch, M. J., Sharp, T. L., Brown, J. J., Perman, W. H., Sun, Y., Motekaitis, R. J., Martell, A. E.: Magn. Reson. Imaging **10**, 903 (1992)
8. Weissleder, R., Heautot, J. F., Schaffer, B. K., Nossiff, N., Papisov, M. I., Bogdanov, A., Brady, T. J.: Radiology **191**, 225 (1994)
9. Gallez, B., Bacic, G., Swartz, H. M.: Magn. Reson. Med. **35**, 14 (1996).
10. Liu, G.-C., Wang, Y.-M., Jaw, T.-S., Chen, H.-M., Sheu, R.-S.: J. Formosan Med. Assoc. (Taiwan) **92**, 359 (1993).
11. Denzler, F.-O., Lebedev, N. A., Novgorodov, A. F., Rösch, F., Qaim, S. M.: Appl. Radiat. Isot. **48**, 319 (1997).
12. Atkins, H. L., Som, P., Fairchild, R. G., Hui, J., Schachner, E., Goldman, A., Ku, T.: Radiology **133**, 769 (1979).
13. Ku, T. H., Richards, P., Strang, Jr., L. G., Prach, T.: Radiology **132**, 475 (1979).
14. Atcher, R. W., Friedman, A. M., Huizenga, J. R., Rayudu, G. V. S., Silverstein, E. A., Turner, D. A.: J. Nucl. Med. **21**, 565 (1980).
15. Atcher, R. W., Friedman, A. M., Huizenga, J. R.: Int. J. Nucl. Med. Biol. **7**, 75 (1980).
16. Herscheid, J. D. M., Vos, C. M., Hoekstra, A.: Int. J. Appl. Radiat. Isot. **34**, 883 (1983).
17. Lambrecht R. M.: Radiochim. Acta **34**, 9 (1983).
18. Knapp, Jr., F. F., Butler, T. A. (Eds.): *Radionuclide Generators - New Systems for Nuclear Medicine Applications*. ACS Symposium Series No. 241, Am. Chem. Soc., Washington D.C., USA (1984).
19. Smith-Jones, P., Schwarzbach, R., Weinreich, R.: Radiochim. Acta **50**, 33 (1990).
20. Bläuenstein, P., Pellikka, R., Schubiger, P. A.: Appl. Radiat. Isot. **48**, 1097 (1997).
21. Cogneau, M., Gilly, L., Cara, J.: Nucl. Phys. **79**, 203 (1966).
22. Lambrecht, R. M., Wolf, A. P.: J. Labelled Cpd. Radiopharm. **16**, 129 (1979)
23. Hichwa, R. D., Nickles, R. J.: IEEE Trans. Nucl. Sci. IEEE Trans. Nucl. Sci. **NS-28**, 1924 (1981).
24. Hichwa, R. D., Daube, M. E., R.J. Nickles: J. Labelled Cpd. Radiopharm. **18**, 227 (1981).
25. Harper, P. V., Lathrop, K. A., Ryan, J. W.: Quantitative studies in radiopharmaceutical science, Manganese-51 for myocardial localization. In: *Nuclear medicine and imaging research*. (Beck, R. N., Cooper, M. D. Eds.), Progress Report DOE/EV/10359–3, January 1 (1980)–December 31 (1982), The Franklin McLean Memorial Research Institute, University of Chicago, USA (1982).
26. Harper, P. V., Lathrop, K. A., Ryan, J. W.: Quantitative studies in radiopharmaceutical science, A.2 Production of manganese-51. In: *Nuclear medicine and imaging research*. (Beck, R. N., Cooper, M. D. Eds.), Progress Report DOE/EV/10359–4, January 1–December 31, The Franklin McLean Memorial Research Institute, University of Chicago, USA (1983).
27. Daube, M. E., Nickles, R. J.: Int. J. Nucl. Med. Biol. **12**, 303 (1985)
28. Browne, E., Firestone, R. B.: *Table of Radioactive Isotopes*. (Shirley, V. S. Ed.), John Wiley & Sons, New York, USA (1986).
29. Holleman, A. F., Wiberg, N.: *Lehrbuch der Anorganischen Chemie*. Walter de Gruyter & Co., Berlin, Germany (1995).
30. Strelow, F. W. W., Weinert, C. H. S. W., Eloff, C.: Anal. Chem. **44**, 2352 (1972).
31. Klein, A. T. J., Rösch, F., Qaim, S. M.: J. Electrochem. Soc. **146**, 4526 (1999)
32. Klein, A. T. J.: Produktion von n.c.a. ^{51}Mn zur *in vivo* PET-Evaluierung von Kontrastmitteln für die Margnetresonanztomographie (MRT). Ph.D. Dissertation, Universität zu Köln, Germany (1997) and Report Jül-3553, FZ Jülich, Germany (1998).
33. Merchel, S.: Über die Wechselwirkung der kosmischen Strahlung mit extraterrestrischer Materie: Radiochemische Bestimmung der Produktionsraten von kosmogenen langlebigen Radionukliden in Meteoriten. Ph.D. Dissertation, Universität zu Köln, Germany (1998).
34. Taube, H.: Chem. Rev. **50**, 69 (1952)
35. Basolo, F., Pearson, R. G.: *Mechanisms of Inorganic Reactions*. 2nd ed., John Wiley & Sons, New York, USA (1967).
36. Theopold, K. H.: Chromium: Inorganic & Coordination Chemistry. In: King, R. B.: *Encyclopedia of Inorganic Chemistry*. Vol. 2, John Wiley & Sons, Chichester, UK (1994).
37. Martell, A. E., Smith, R. M.: *Critical Stability Constants*. Plenum, New York, USA (1976).
38. Falbe, J., Regitz, M. (Eds.): *Pömpp Chemie Lexikon*. 9. Aufl., Georg Thieme, Stuttgart, Germany (1992).
39. Sillén, L. G., Martell, A. E.: *Stability Constants of Metal-Ion Complexes*. Special publication No. 25, pupplement No. 1 to special publication No. 17, The Chemical Society, Burlington House, London, UK (1971).
40. Atkins, P. W.: *Physikalische Chemie*. VCH, Weinheim, Germany (1988).
41. DeCorte, F., Van den Winkel, P., Speecke, A., Hoste, J.: Anal. Chim. Acta **42**, 67 (1968)-
42. Chakravorty, M., Khopkar, S. M.: Chromatographia **12**, 44 (1979).
43. Morie, G. P., Sweet, T. R.: J. Chromatogr. **16**, 201 (1964)
44. Koprda, V., Fojtík, M.: Chemické Zvesti (Bratislava) **19**, 294 (1965).
45. Koprda, V., Fojtík, M.: Chemické Zvesti (Bratislava) **22**, 333 (1968).
46. Van Horne, K.C. (Ed.): *Festphasenextraktion*. ICT GmbH, Frankfurt (Main), Germany (1993).
47. Weiner, R., Schiele, V.: Fresenius' Z. Anal. Chem. **169**, 217 (1959).
48. Mulokozi, A. M.: Analyst **97**, 820 (1972).
49. Dean, J. A., Cain Jr., C.: Anal. Chem. **29**, 530 (1957).
50. Johnson, D. A., Lott, P. F.: Anal. Chem. **35**, 1705 (1963).
51. Svoboda, K., Mudrová, B.: Radiochim. Acta **7**, 57 (1967).
52. Maxwell, R. D., Gile, J. D., Garrison, W. M., Hamilton, J. G.: J. Chem. Phys. **17**, 1340 (1949).
53. Haymond, H. R., Garrison, W. M., Hamilton, J. G.: J. Chem. Phys. **19**, 382 (1951).
54. Fessler, A., Qaim, S. M.: Radiochim. Acta **72**, 121 (1996).
55. Greene, M. W., Lebowitz, E., Richards, P., Hillman, M.: Int. J. Appl. Radiat. Isot. **21**, 719 (1970).
56. Lyster, D. M., Thaller, R., Vincent, J. S., Dougan, H., Morrison, R. T.: Production and Purification of ^{52}Fe. In: Lambrecht, R. M., Morcos, N.: *Applications of Nuclear and Radiochemistry*. Pergamon, New York, USA (1982).
57. Zweit, J., Downey, S., Sharma, H.: Appl. Radiat. Isot. **39**, 1197 (1988).
58. Amphlett, C. B., McDonald, L. A., Redman, M. J.: J. Inorg. Nucl. Chem. **6**, 236 (1958).
59. Duwell, E. J., Shepard, J. W.: J. Phys. Chem. **63**, 2044 (1959).
60. Perrin, D. D.: *Stability Constants of Metal-Ion Complexes, Part B: Organic Ligands*. IUPAC Chemical Data Series – No. 22, Pergamon, Oxford, UK (1979).