TRISKEM
Expertise in Separation Chemistry

PRODUCT SHEET

ZR Resin

Main Applications

- Separation of zirconium
- Separation of gallium
- Separation of germanium
- Separation of titanium

Packing

Order N°.	Form	Particle size
ZR-B25-A, ZR-B50-A, ZR-B100-A, ZR-B200-A	25g, 50g, 100g and 200g bottles ZR resin	100-150 µm
ZR-B25-S, ZR-B50-S, ZR-B100-S, ZR-B200-S	25g, 50g, 100g and 200g bottles ZR resin	50-100 µm
ZR-R10-S	10 2 mL ZR Resin cartridges	50-100 µm
ZR1-R10-S	10 1 mL ZR Resin cartridges	50-100 µm
ZR0.3-R10-S	10 0.3 mL ZR Resin cartridges	50-100 µm

Physical and chemical properties

Density: 0.34 g dry ZR Resin/mL

Conditions of utilization

Recommended T of utilization : 20-25°C

Flow rate: A grade: 0.6 – 0.8 mL/min, utilization with vacuum or with pressure for s grade resin

Storage: Dry and dark, T<25°C. Storing the resin at 2 – 8°C may increase the shelf-life of the resin. It is however very important to allow the resin to get back to RT before use.

For additional information see enclosed literature study

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ZR RESIN

The ZR Resin is based on the hydroxamate functionality frequently used for the separation of zirconium, especially from Y target materials, for later use in radiopharmaceutical applications.
Dirks et al.[1] characterized the resin with respect to its selectivity for selected elements in HNO_3, HCl and oxalic acid; results are summarized in Figures 1 – 5.

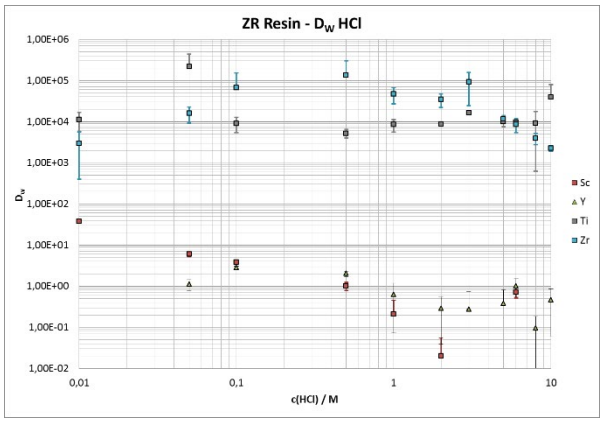

Figure 1: D_W values, ZR Resin, HCl, various elements

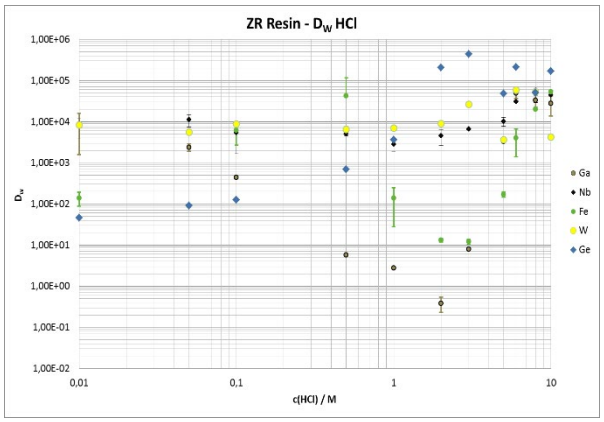

Figure 2: D_W values, ZR Resin, HCl, various elements

The ZR Resin shows high selectivity for Zr, Ti and Nb over a wide range of HCl concentrations (0.01M – 10M), Fe(III) is strongly retained at low and elevated HCl concentrations, retention is weak from 1 – 6M HCl. As expected, the resin shows very little selectivity for Sc and Y, a separation e.g. of Zr from Y and of Ti from Sc seems thus feasible.

The resin further shows quite interesting selectivity with respect to Ga and Ge.

Ga is very well retained at low HCl concentrations (≤0.1M) as well as at high concentrations (≥5M HCl), while Zn e.g. is not retained at all. At HCl concentrations in-between, particularly at 1-2M HCl it is not retained. Ge on the other hand is very well retained at HCl concentrations >0.1M. Especially at 2M HCl the selectivity for Ge over Ga is very high.

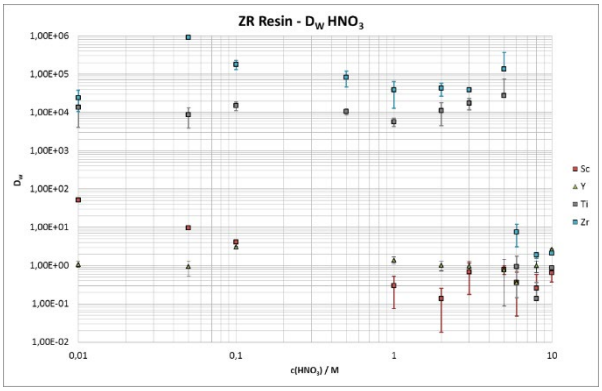

Figure 3: D_W values, ZR Resin, HNO_3, various elements

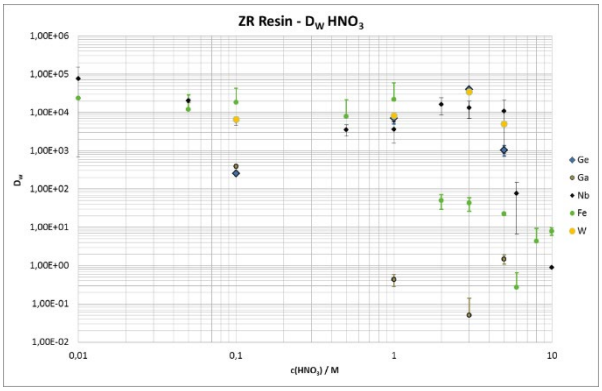

Figure 4: D_W values, ZR Resin, HNO_3, various elements

The resin shows rather similar selectivity in HNO_3. Zr, Ti and Nb are well retained up to 5M HNO_3, Fe(III) is well retained up to 1M HNO_3. At higher HNO_3 concentrations the nitric acid starts decomposing the extractant, as indicated by a colour change of the resin from white to brown; accordingly, the resin shows no significant selectivity towards the tested cations under these conditions. As in HCl, Y and Sc show no significant retention on the ZR Resin in HNO_3.

It should be noted that the ZR Resin also shows high selectivity for Ge over Ga (and Ni/Co) at elevated HNO_3 concentrations.

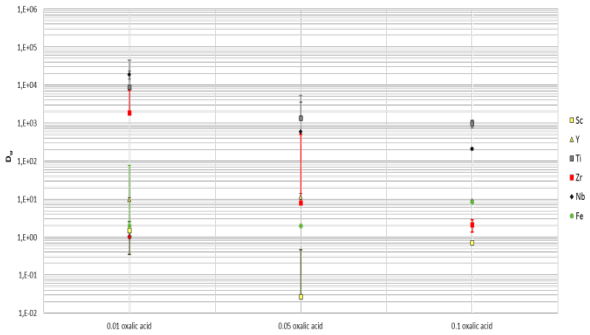

Figure 5: D_W values, ZR Resin, oxalic acid, various elements

Oxalates are very strong complexing agents for Zr, accordingly they are very frequently used for the elution of Zr.
It could be shown that oxalic acid concentrations above 0.05M lower the D_W value of Zr on the ZR Resin strongly; they are thus suitable eluting agents for Zr. It was further observed that Nb shows rather elevated D_W values even at 0.05M oxalic acid, indicating that Zr and Nb may be separated by adjusting the oxalic acid concentration accordingly.

Based on obtained D_W values several elution studies were performed[1, 2] with main focus on the use of the resin in the context of radionuclide production for radiopharmaceutical use.

As indicated by the D_W values, the ZR Resin will retain Zr over a range of HCl concentrations. The rinsing conditions were kept close to the conditions suggested by Holland et al.[3]: after loading the resin it is first rinsed with 4 x 2.5 mL 2M HCl, followed by an additional rinse with 4 x 2.5 mL water. Zr is finally eluted using 0.05M oxalic acid or higher.

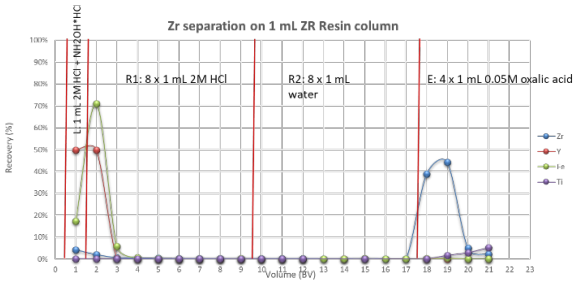

Figure 6: Elution study ZR Resin, 100 mg, various elements, fractions analysed by ICP-MS

Under the given conditions a very clean separation of Zr from Y, Ti and Fe was obtained. Y and Fe are removed during the loading and rinsing of the ZR Resin, while Ti remains retained on the resin. Zr can be recovered quantitatively in ~2 bed volumes (BV) of 0.05M oxalic acid. High chemical yields could be obtained even in presence of up to 300 mg stable Y (using 100 mg ZR Resin).

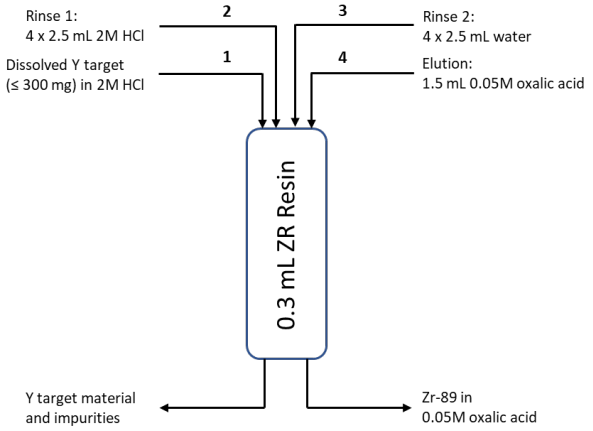

Figure 7: suggested method for the separation of Zr from Y targets (≤ 300 mg) using the ZR Resin.

The ZR Resin is currently also being tested for use in radioanalytical applications such as the quantification of Zr-93, as well as, in combination with the TK400 Resin, the separation of Fe/Nb/Mo, e.g. in decommissioning samples.

Another increasingly important use of the ZR Resin is the purification of Ga-68 from irradiated Zn targets. The production of Ga-68 via the irradiation of Zn-68 (as liquid or solid targets) on a cyclotron is indeed increasingly finding use as an alternative to Ge-68 generator produced Ga-68, as it allows frequent production of high activities.

As shown in Fig. 2 and 4 the ZR Resin retains Ga very strongly in dilute HCl and HNO_3, as well as in HCl of elevated concentration (≥ 5M HCl). Zn on the other hand is not retained under any of these conditions. This selectivity allows its use for the separation of Ga-68 (and Ga-67) from irradiated Zn targets - liquid targets (typically dilute HNO_3) as well as solid targets (typically dissolved in HCl of high concentration).
HCl between 1M and 2M on the other hand is very suitable for Ga elution as its retention is particularly low under these conditions.

Fig. 8 shows a typical example of such a separation. While Zn, and other typical impurities such as Cu and Ni, are not retained on the ZR Resin (in this example from high HCl) Ga is very well retained. A clean Ga fraction is then obtained by elution of Ga e.g. with 1.5M HCl.

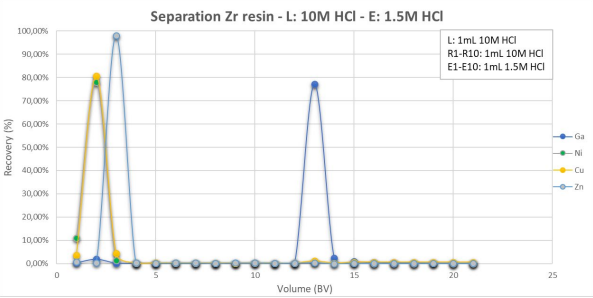

Figure 8: Elution study, Ga separation on ZR Resin, various elements, fractions analysed by ICP-MS

This Ga-68 containing 1.5M HCl solution is too acidic for direct use in labelling or injection. Instead of converting the solution to more suitable conditions e.g. via evaporation and redissolution it is possible to use another resin for this step, the TK200 Resin. More information on the TK200 Resin selectivity may be found in its product sheet[4], in this context the most important fact is that it retains Ga well in the range of 1 – 2M HCl, while it allows for Ga elution in dilute HCl or water, making it very suitable for this required conversion.

It should be noted though that while other impurities like Cu are very well removed during load and rinse on the TK200, remaining traces of Zn are only partially removed, accordingly a clean separation on the ZR Resin upfront is very important.
Fig. 9 shows a typical Ga conversion on TK200[2].

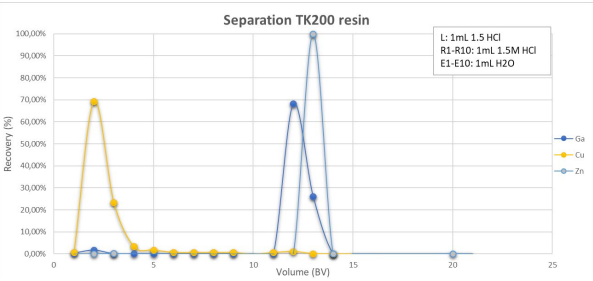

Figure 9: Elution study, Ga conversion on TK200, various elements, fractions analysed by ICP-MS

Several publications describe the use of the combination of ZR Resin and TK200 for the separation of Ga-68 from liquid Zn targets[5-7]. The publication by Rodnick et al.[6] is particularly interesting as it describes the use of a modified rinse on the TK200 cartridge (2M NaCl/0.13M HCl) instead of the usual rinse with HCl. This allows for recovering the final Ga fraction at a better-defined HCl concentration during elution. Fig. 10 schematically shows the separation method they developed.

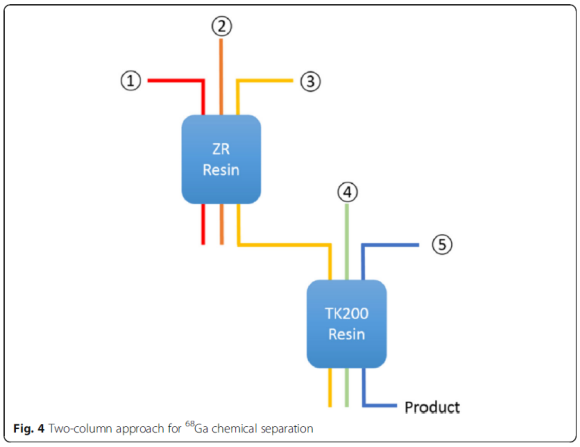

Fig. 4 Two-column approach for ^{68}Ga chemical separation

Table 1 High level schemes of [^{68}Ga]$GaCl_3$ purifications

	Scheme A*	Scheme B
① ZR Load	< 0.1 M HNO_3	
② ZR Wash	15 mL 0.1 M HNO_3	
③ ZR Elution / Trapping on TK200	5–6 mL ~ 1.75 M HCl	
④ TK Wash	–	3.5 mL 2.0 M NaCl in 0.13 M HCl
⑤ TK Elution	H_2O	1–2 mL H_2O followed by dilute HCl to formulate

*Process as reported previously (Nair et al. 2017)

Figure 10: Scheme of Ga-68 separation from liquid Zn targets using ZR Resin and TK200 Resin, taken from Rodnick et al.[6]

Compared to liquid targets the irradiation of solid Zn targets allows for obtaining higher Ga-68 activities per production run.
Thisgaard et al.[7] describe the production of 194 GBq Ga-68 (at end of purification) as [^{68}Ga]$GaCl_3$ of high purity, and it's subsequent successful use for the labelling of PSMA-11 and DOATATE. The authors used a three-resin method for the separation. An additional LN Resin cartridge is used between the ZR Resin and the TK200 Resin to further remove potentially present impurities, particularly Fe.

The ZR Resin further shows very interesting selectivity for Ti, especially with respect to Sc.
Fig. 11 shows an example of a Ti/Sc separation performed on the ZR Resin, while Sc is not retained from 10 M HCl Ti is fixed very well. 0.1M citric acid may then be used to elute Ti from the resin. However, the elution requires up to 10 bed volumes (BV) of the eluent or more. Beside citric acid, hydrogen peroxide or oxalic acid of elevated concentration may also be employed.

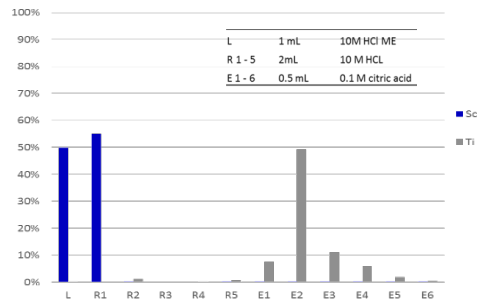

Figure 11: Ti/Sc separation on ZR Resin (0.3 mL), fractions analysed by ICP-MS

As Ti is retained over a very wide range of HCl concentrations (fig. 2), including dilute HCl, its potential for use as support for a Ti/Sc generator was also evaluated initially. In order to do so a 100 mg ZR Resin column (0.3 mL) was loaded with a small volume of a solution containing Ti and Sc. The column was then rinsed five times with 1 mL 0.01M HCl, followed by 10 rinses with 5 mL 0.01M HCl. As shown in Figure 12, Sc is easily removed in a small volume of dilute hydrochloric acid whereas Ti remains retained throughout the experiment, the general selectivity of a generator is thus given.

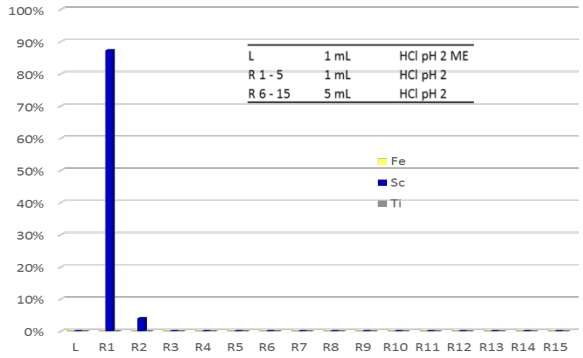

Figure 12: Elution study on 100 mg ZR Resin, Ti and Sc, load from 0.01M HCl, repeated elutions, fractions analysed by ICP-MS

Radchenko et al.[9] examined the system in greater detail and using real, irradiated samples. They confirmed the ZR Resins selectivity for Ti over Sc, fig. 13 shows the K_d values the author obtained.

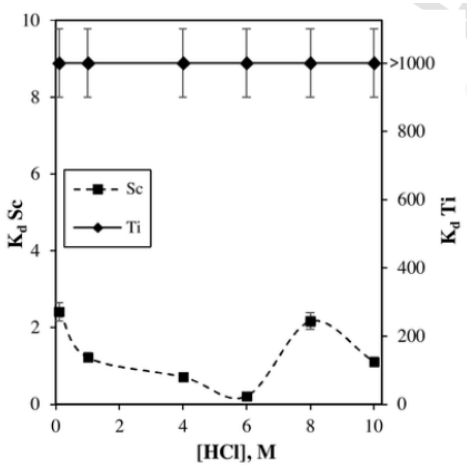

Figure 13:Kd values for Sc and Ti in HCl on ZR Resin, taken from Radchenko et al.[9]

Based on these values they developed a separation method for the purification of Ti, to be more precise Ti-44, from irradiated Sc targets of elevated size (4 g). Fig. 14 shows the elution profile they obtained.

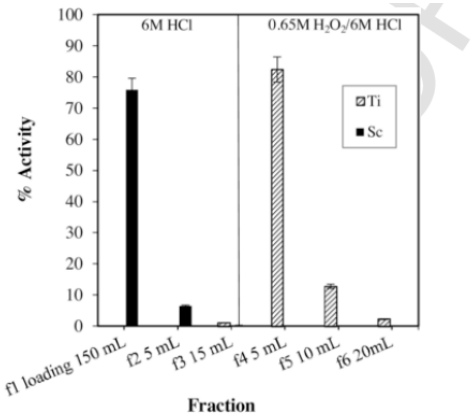

Figure 14: Ti/Sc elution profile on ZR Resin, irradiated 4g Sc target, taken from Radchenko et al.[9]

As may be seen a clean Ti separation from Sc was obtained. The Ti-44 was obtained as an HCl/H_2O_2 solution.

The authors used the purified Ti-44 solution for the preparation of two types of Ti-44/Sc-44 generators, one direct flow generator and, the preferred option according to the authors, one 'forward/reverse flow' generator (fig. 15).

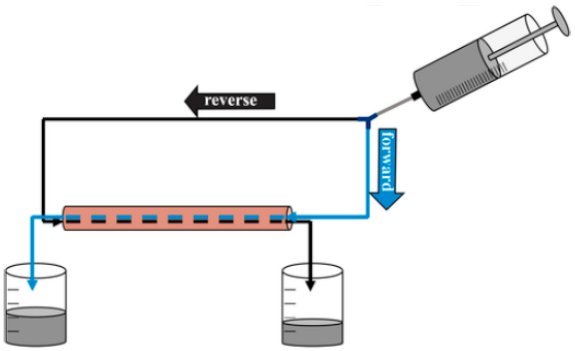

Figure 15: Schematic of a forward/reverse flow radionuclide generator, taken from Radchenko et al. [9]

Especially the 'forward/reverse flow' generator showed very promising results with stable very low Ti breakthrough and high Sc elution yields. The obtained Sc-44 was successfully used to perform DOTA labelling with high yields, further indicating its high purity.

Malinconico et al.[10] also used the ZR Resin to produce Ti-45 from irradiated Sc-45 targets.

Besides for the purification of Ga-68 from Zn targets the ZR Resin may actually also be used for the separation of Ge-68 from irradiated GaNi or GaCo targets. As discussed before, while Ga is very well retained at low mineral acid concentrations (typically ≤0.1M) and at high HCl concentrations, it is not retained at medium high HCl and HNO_3 concentrations, and medium to high H_2SO_4 concentrations. Ge on the other hand is very well retained at elevated mineral acid concentrations. Fig. 2 and 4 show that especially between 1M – 3M HCl and HNO_3 the Ge retention is significantly higher than Ga retention.
It could be shown[2] that the same is true for e.g. 5M H_2SO_4. The ZR Resin further shows no selectivity for Ni or Co under these conditions.

While the selectivity for Ge over Ga is very high in HCl its use for Ge separations is often avoided due to the high volatility of $GeCl_4$. In H_2SO_4 on the other hand Ge is not volatile, it further allows an efficient dissolution of typically employed target materials. Accordingly, a method for the separation of Ge-68 from multi gram irradiated GaNi or GaCo targets is currently being optimized.

The method is based on two subsequent purification steps on ZR Resin[2]. First the dissolved target is adjusted to 5M H_2SO_4 and then loaded onto a 2 mL ZR Resin cartridge. After rinsing with 5M H_2SO_4 and purge with air for acid removal Ge is eluted with dilute citric acid. The Ge fraction is again adjusted to 5M H_2SO_4 and further purified on a 1 mL ZR Resin cartridge. Ge is once more recovered in dilute citric acid. In order to obtain the final product in dilute HCl (typically 0.05M HCl) the Ge is converted from citric acid to dilute HCl by adjusting it to 9M HCl, loading onto a Guard Resin[11] cartridge, followed by elution with water or dilute acid. Further optimisation of the method is currently on-going.

Bibliography

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