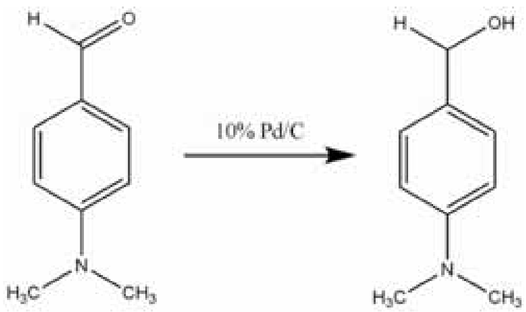
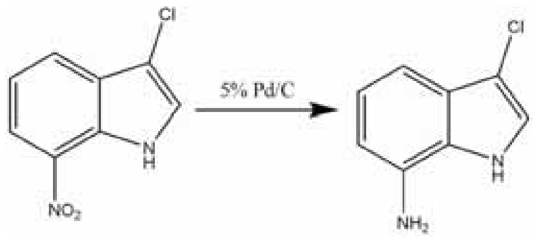
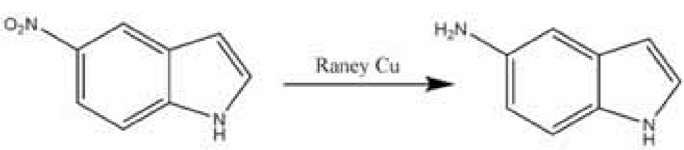
Application note for ScavCarts™ - using H-Cube®

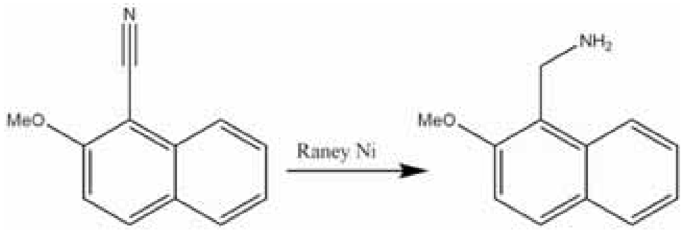
Metal contamination is a major problem for the pharmaceutical and fine chemical industries. A large amount of time and resource is spent purifying compounds after catalytic steps, so that the metal concentration is within the acceptable limit. Generally, the acceptable limit is 0.05-10 ppm, for those metals that are utilized in hydrogenation. Scavenger resins are often used for metal contamination purification. In this application note, we will demonstrate how the H-Cube® and a scavenger cartridge (ScavCart™) may be combined to perform a reaction and purification in 1 step.

EXAMPLES FOR HYDROGENATION REACTIONS









The H-Cube® is a continuous flow hydrogenation reactor. During the reaction process, the substrate is mixed with hydrogen and passed through a catalyst cartridge (CatCart®). The reaction takes place on the catalyst before flowing out of the cartridge and into a collection vial. All solid catalyst remains behind in the cartridge, but any dissolved metal must be removed through purification before proceeding to the next step. This is typically done using prep-HPLC and is a time consuming and costly process. Not to mention the environmental impact in the amount of solvent used during the purification process.

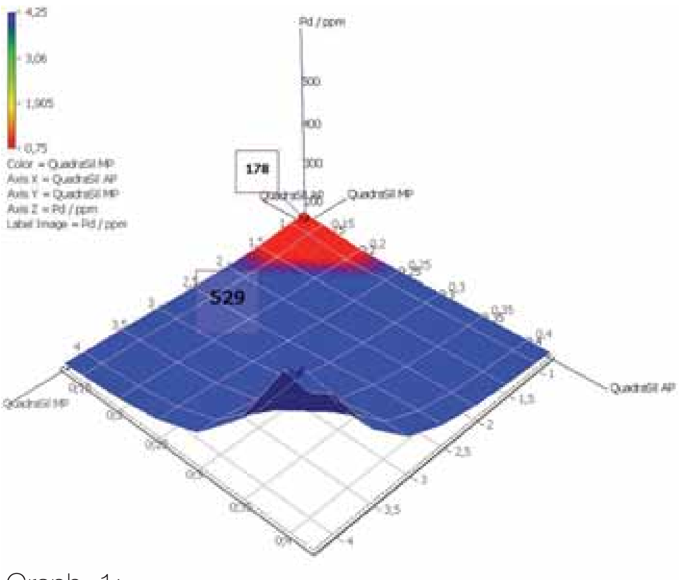
At ThalesNano, we have integrated the purification step into the reaction process. A scavenger resin cartridge (ScavCart™) is inserted into the reaction line just before the reaction mixture flows into the collection vial. Any dissolved metal from the CatCart® is adsorbed by the scavenger resin, purifying the reaction mixture before it is collected. Further purification is not necessary, saving time, value, and money. The experiments below detail the ScavCarts™ capacity to remove dissolved metals from the reaction mixture.

STANDARD EXPERIMENTAL PROTOCOL

A metal-containing solution is passed through the scavenger-filled cartridge using H-Cube® at atmospheric pressure, room temperature and a flow rate of 1 mL/min in no hydrogen mode. The metal content was measured both before the reaction and afterwards by ICP-MS analysis.

PALLADIUM SCAVENGING

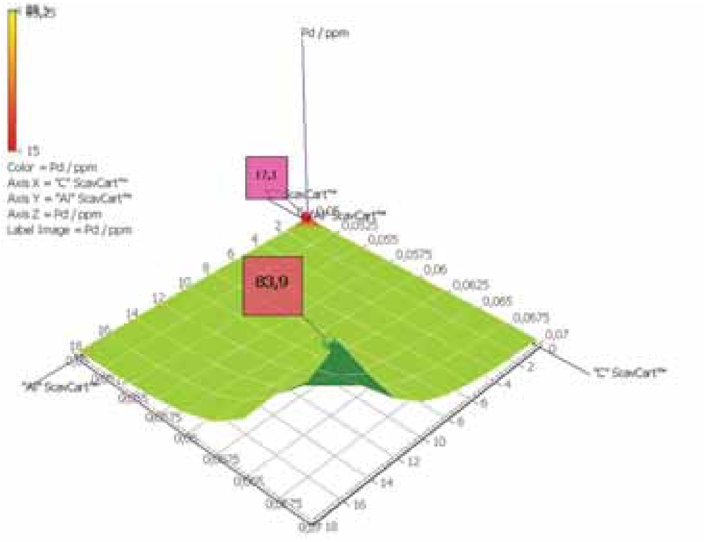
A standard solution of 1000 ppm $Pd(NO_3)_2$ in 1M HNO_3 was diluted with water and the pH was adjusted to 7 using solid Na_2CO_3. Two different concentrations of Pd metal were used to determine the absorption capacity at different concentrations. The exact concentration of the starting material was measured by ICP-MS and the solution was passed through the H-Cube® containing a particular ScavCart™. Four different scavengers were tested: QuadraSil™ AP, QuadraSil™ MP, Metal scavenger Phosphotungstic acid modified carbon („C") and Metal scavenger Phosphotungstic acid modified alumina („Al") scavengers. A 10 mL analytical sample was taken in all cases to measure the Pd content by ICP-MS before and after the scavenging.



Graph. 1:
Results of Pd scavenging with QuadraSil™ AP, QuadraSil™ MP scavengers (in the boxes: Pd content of starting material in ppm)

	c_{Pd} / ppm	
Starting solution metal concentration	178	529
After QuadraSil™ AP / ppm	0.13 (100%)	0.41 (100%)
After QuadraSil™ MP / ppm	0.83 (100%)	4.23 (99%)

Table 1.:
Results of Pd scavenging with % of scavenged metal



Graph. 2:
Results of Pd scavenging with Metal scavenger Phosphotungstic acid on modified carbon („C") and Metal scavenger Phosphotungstic acid on modified alumina („Al") scavengers (in the boxes: Pd contents of starting material in ppm)

	c_{Pd} / ppm	
Starting solution concentration	17.10	83.90
After Metal scavenger Phosphotungstic acid modified carbon („C") / ppm	0.05 (100%)	0.07 (100%)
After Metal scavenger Phosphotungstic acid modified alumina („Al") / ppm	0.09 (100%)	16.60 (80%)

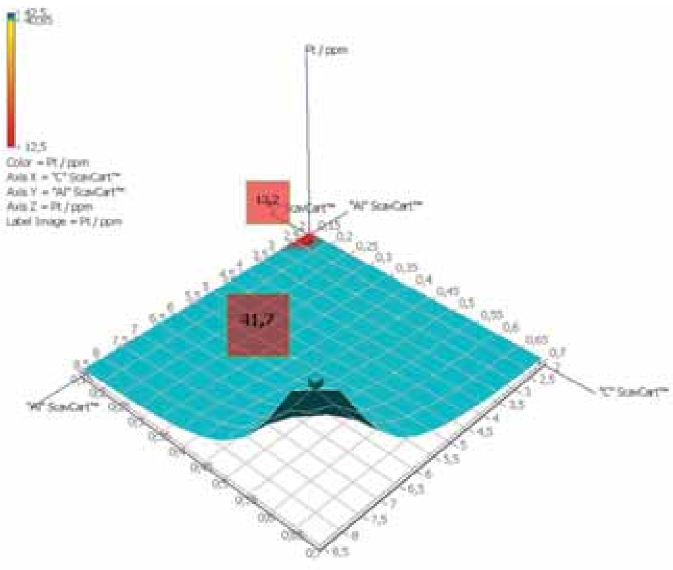
Table 2.:
Results of Pd scavenging with % of scavenged metal

RESULTS OF PALLADIUM SCAVENGING

All scavengers eliminated 80 - 99.9% of Pd. As seen in Graph. 1, testing the solutions with 178 and 529 ppm Pd content using QuadraSil™ MP and QuadraSil™ AP scavengers, the concentration of the metal was dramatically reduced. The same results can be seen in Graph. 2 when solutions with smaller amounts of Pd were passed through the ScavCart™ using the "C" and "Al" scavengers.

PLATINUM SCAVENGING

Standard concentration of 1000 mg/L $PtCl_6$ in 2 M HCl was diluted with water and the pH of the starting material was set to 7-8 with NaOH. Metal scavenger Phosphotungstic acid modified carbon („C") and Metal scavenger Phosphotungstic acid modified alumina („Al") were used to eliminate the concentration of the Pt metal. The amount of dissolved Pt present was measured by ICP-MS before and after the solutions were passed though the scavenger filled ScavCarts™ at 25°C, atmospheric pressure and flow rate of 1 mL/min. 10 mL samples were used for analysis.



Graph. 3:
Results of Pt scavenging using Metal scavenger Phosphotungstic acid modified carbon („C") and Metal scavenger Phosphotungstic acid modified alumina („Al") (in the boxes: Pt content of starting material in ppm)

	c_{Pt} / ppm	
Starting solution concentration	13.20	41.70
After Metal scavenger Phosphotungstic acid modified carbon („C") / ppm	0.17 (99%)	0.69 (98%)
After Metal scavenger Phosphotungstic acid modified alumina („Al") / ppm	2.32 (82%)	8.43 (80%)

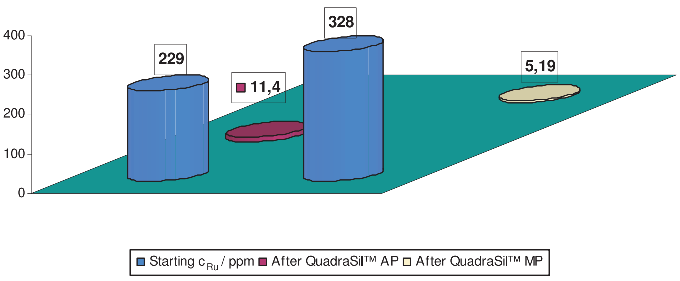
Table 3.:
Results of Pt scavenging with the % of scavenged metal

RESULTS OF PLATINUM SCAVENGING

The same scavengers that were used in the Pd scavenging where used for the Pt scavenging, namely Metal scavenger Phosphotungstic acid modified carbon („C") and Metal scavenger Phosphotungstic acid modified alumina („Al") The results of scavenging can be seen in Table 3. and Graph. 3. which indicate that these scavengers can also, eliminate 80 - 98% of the Pt residues from a solution with low metal content.

RUTHENIUM SCAVENGING

Standard concentration of 1000 mg/L $RuCl_3$ in 1 M HCl was diluted with water and the pH was adjusted to 8 with solid Na_2CO_3. The ruthenium was scavenged by QuadraSil™ AP and QuadraSil™ MP. The amount of Ru was measured by ICP-MS collecting 10 mL samples before and after the solutions were passed though the scavenger filled ScavCarts™ at 25°C, atmospheric pressure and flow rate of 1 mL/min.



Graph. 4.
Result of Ruthenium scavenging with QuadraSil™ AP and QuadraSil™ MP scavengers

	c_{Ru} / ppm	
Starting solution concentration	229	358
After QuadraSil™ AP / ppm	11.40 (95%)	-
After QuadraSil™ MP / ppm	-	5.19 (98%)

Table 4.:
Results of Ru scavenging with the % of scavenged metal

RESULTS OF RUTHENIUM SCAVENGING

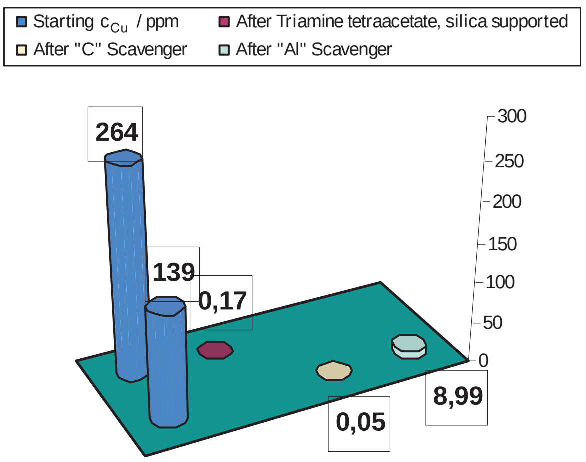
The ruthenium content of two solutions with different Ru concentrations were scavenged with QuadraSil™ AP and QuadraSil™ MP scavengers. Both of the used scavengers eliminate more than 95% of the metal content from the solution.

COPPER SCAVENGING

Solution with standard concentration of 1000 ppm high purified copper in 2 w/w% $cHNO_3$ was diluted with water and was passed through each scavenger-filled cartridge at a flow rate of 1 mL/min, atmospheric pressure and at room temperature.

RESULTS OF COPPER SCAVENGING

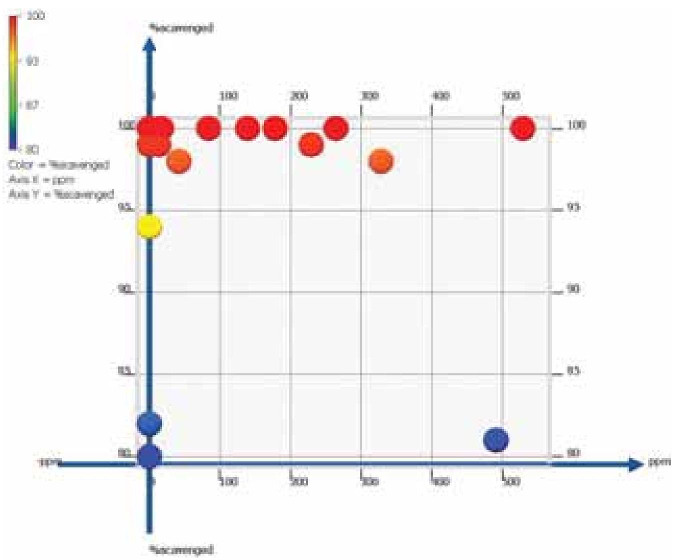
As displayed in Graph. 5 and Table 5. these scavengers dramatically reduced the amount of copper present in the starting solution.



Graph. 5:
Copper scavenging using silica-supported triamine tetraacetate, Metal scavenger Phosphotungstic acid modified carbon („C") and Metal scavenger Phosphotungstic acid modified alumina („Al")

	c_{Cu} / ppm		
Starting solution concentration	264	491	139
After Triamine tetraacetate silica supported / ppm	0.17 (100%)	-	-
After Metal scavenger Phosphotungstic acid modified carbon („C") / ppm	92 (81%)	-	-
After Metal scavenger Phosphotungstic acid modified alumina („Al") / ppm	-	0.05 (100%)	8.99 (94%)

Table 5.:
Results of Cu scavenging with % of scavenged metal



Graph. 6.:
Results of ScavCarts™ with % of scavenged metal

CONCLUSION

The results demonstrate that the scavengers tested are highly effective in reducing the amount of dissolved metals. They were effective in reducing the palladium, platinum, nickel and copper concentrations by up to 99%.

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