

Large volume CIM[®] chromatographic monoliths – scalability and uniformity



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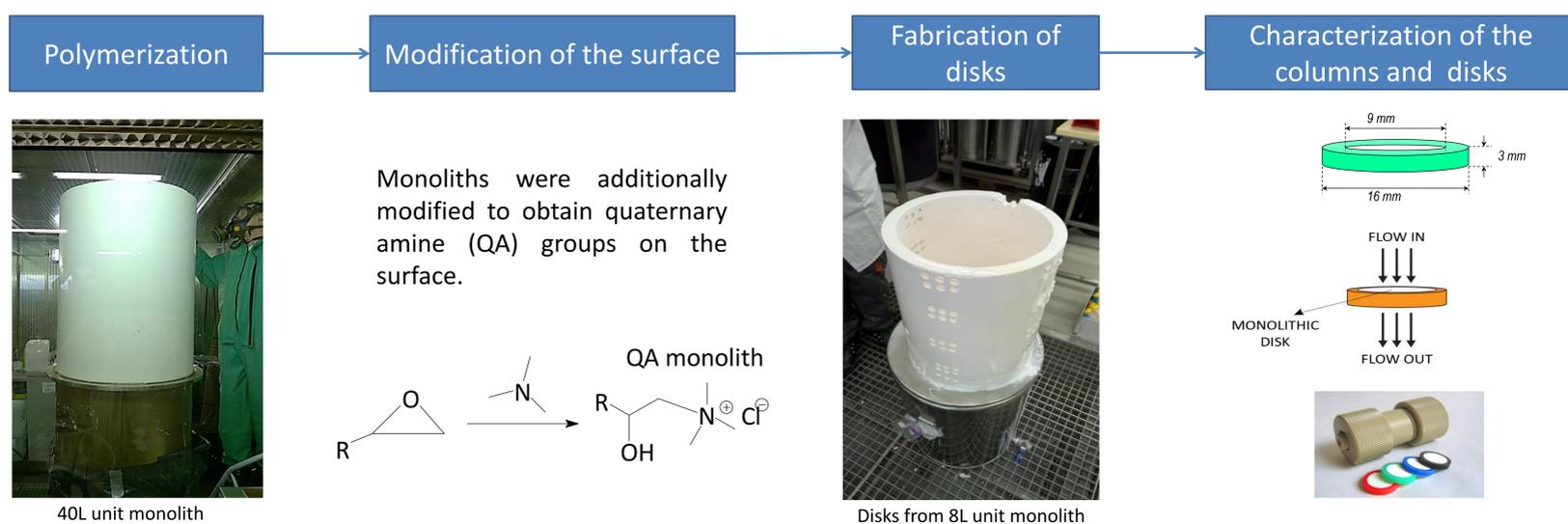
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INTRODUCTION

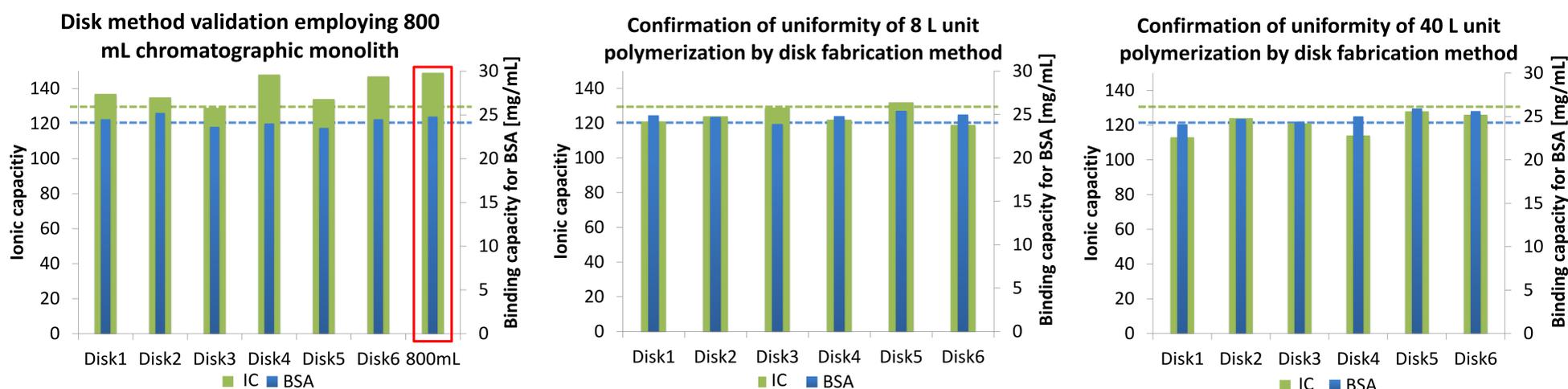
To ensure the desired chromatographic characteristics of the CIM[®] monolithic column at large scales, monolith microstructure morphology, pore size distribution, porosity and surface ligand density should be uniform. To demonstrate the uniformity of large chromatographic monoliths we have developed new testing procedures. By fabricating smaller columns (disks) from different random positions of larger

monolith, non-cGMP compliant chromatographic testing can be applied on the same polymerization batch without affecting the cGMP compliance of large-scale chromatographic monolith. Each individual disk was thoroughly tested and the results were compared to the properties of the large monolith.

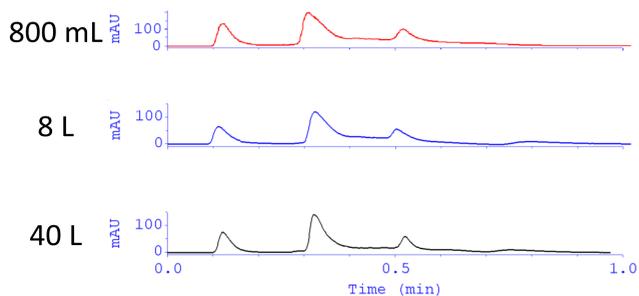
RESULTS



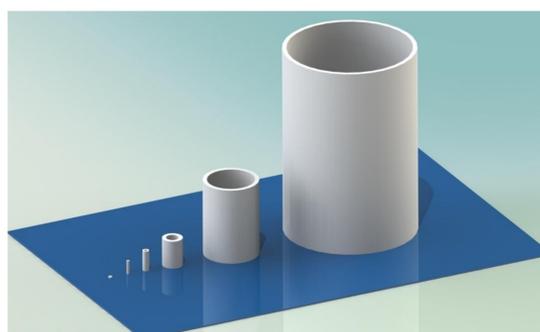
Confirmation of uniformity of large scale polymerization by disk fabrication method (average of BSA (----) and IC (-----) on all scale-up disks



Uniformity of monoliths was tested using chromatographic methods, pore size distribution, porosity and surface ligand density. Those parameters should be uniform and consistent through the entire scale-up of the monoliths.



Comparison – 800 mL, 8 L, 40 L monolith				
Size	Young's module (MPa)	Pore size radius (nm)	Ionic capacity (mM)	DBC for BSA (mg/mL)
800 mL	12.9	1110	139	24.0
8 L	13.1	1050	121	25.0
40 L	12.9	1040	125	24.9



	800 mL	8 L	40 L
I.D. (mm)	65	243	636
O.D. (mm)	105	285	680
Thickness (mm)	20	21	22

We also managed to retain wall thickness and radial geometry for further flow-independent properties of monoliths.

CONCLUSIONS

- An alternative chromatographic testing method for large monoliths (based on fabrication of small disks from the part of large polymer) was developed.
- High correlation in material and chromatographic properties were observed between the disks and large monolith.

- Homogeneity of monoliths at least up to the 40 L bed volume size was proven.
- Further development will follow to direction of producing screening disks from the same polymerization as the large chromatographic monoliths.