OraChrom, Inc.
The Vanguard of Liquid Chromatography.

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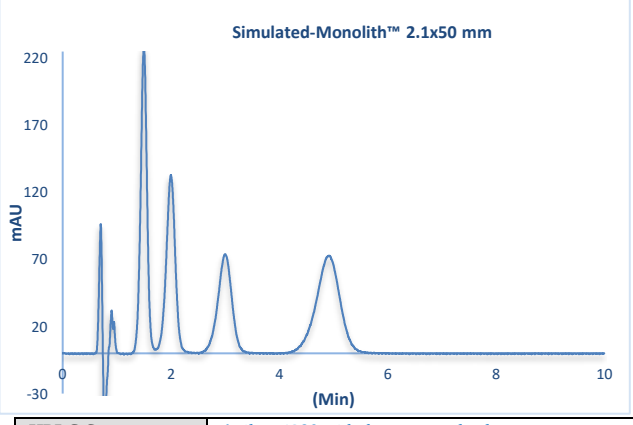
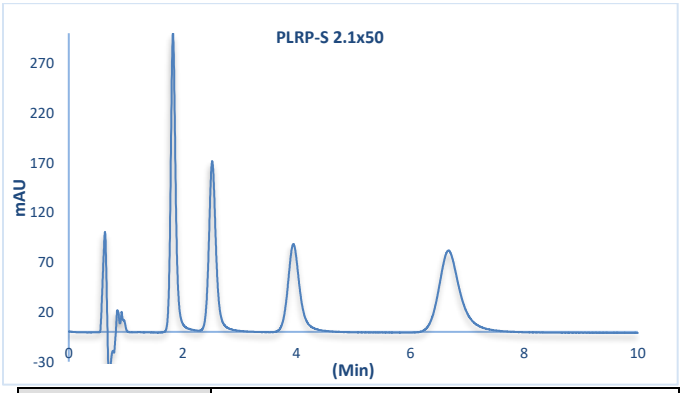
APPLICATION NOTE

Simulated-Monolith™ STYROS® polymerics compared with Pellicular 3 µm polymeric.

The favorable characteristics of Monoliths has given them priority in the realm of chromatography specifically during the manufacturing processes. Their present limitation, however, has prevented them from gaining any noticeable advantage in this sphere except the use of their names as a marketing contrivance or stratagem.
The succinct description of their advantage is to simply replace the slow "diffusive" separation process with the fast "convective" one.
It took SMB (Simulated Moving Bed) chromatography to transform the batch processing in chromatography into a continuous flow processing amenable to automation.
Simulated-Monolith™ is now the vanguard and the long-awaited segment needed to allow automatic processing to get pure biopharmaceuticals, especially vaccines, to provide our universe with it, to fight the spread of the presently persisting virus and any future variants on the horizon.
One of the major advantages of Monoliths is their low back pressure making them ideal in industrial processes.
Additionally, unlike leaching soft gels, high capacities are maintained even at high flow rates.
Here we have chosen narrow bore columns of 2.1 mm ID to compare a polymeric Simulated-Monolith™ with a conventional 3 µm, 100 Å PLRP-S.
This highlights some of the characteristics of Simulated-Monolith™ and compares it with pellicular polymeric particles.

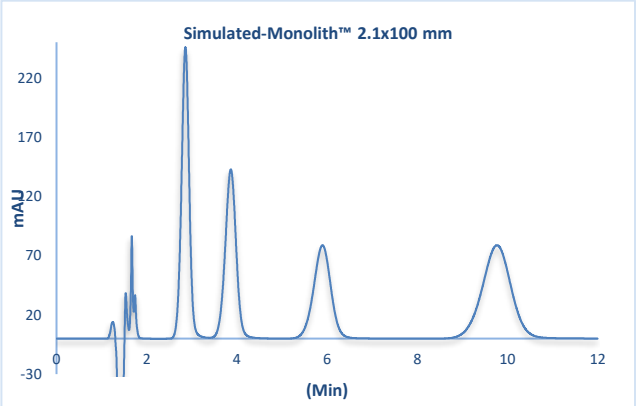


HPLC System.	Agilent 1290 with thermostatted column compartment and binary pump.
Columns	STYROS® Simulated-Monolith™ 1R 2.1 mm X 50 mm (0.173 ml volume)
Mobile phase.	A: 2 % ACN in H20, 0.1 % THF B: 100 % ACN, 0.1 % TFA
Flow rates	0.2 ml/min (> 340 cm/hr of linear velocity on an empty column)
Isocratic	40 % B for 10 min
Temperature	30°C
Detection	254 nm
Injection volume	10 µl
Pressure Drop	40 bars at 0.2 ml/min. System 12 bar.
Sample:	Certified diagnostic test 48270-U Supelco made of 4 parabens, methyl, ethyl, propyl, and butyl parabens.



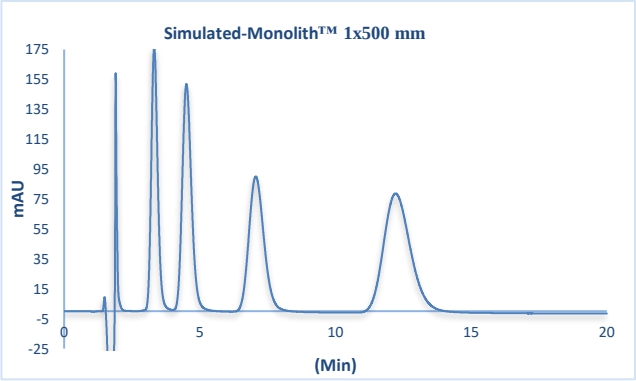
HPLC System.	Agilent 1290 with thermostatted column compartment and binary pump.
Columns	PLRP-S 2.1 mm X 50 mm (0.173 ml volume)
Mobile phase.	A: 2 % ACN in H20, 0.1 % THF B: 100 % ACN, 0.1 % TFA
Flow rates	0.2 ml/min (> 340 cm/hr of linear velocity on an empty column)
Isocratic	40 % B for 10 min
Temperature	30°C
Detection	254 nm
Injection volume	10 µl
Pressure Drop	105 bars at 0.2 ml/min. System 12 bar.
Sample:	Certified diagnostic test 48270-U Supelco made of 4 parabens, methyl, ethyl, propyl, and butyl parabens.

With more than double the back pressure at similar linear flow rates of 340 cm/hr. PLRP-S cannot be supported by process instruments whereas the Simulated-Monolith™ can. With 4,000 to 6,000 angstroms through pores these monoliths are stable and unlike soft gel or any other stationary phase on the market, they do not leach and therefore contaminate the purified products.
Furthermore, the length of the column can be doubled, with the back pressure remaining below pellicular packed columns should the performance need to be increased:



HPLC System.	Agilent 1290 with thermostatted column compartment and binary pump.
Columns	STYROS® 1R Simulated-Monolith™ 2.1 mm X 100 mm (0.346 ml volume)
Mobile phase.	A: 2 % ACN in H20, 0.1 % THF B: 100 % ACN, 0.1 % TFA
Flow rates	0.2 ml/min (> 340 cm/hr of linear velocity on an empty column)
Isocratic	40 % B for 12 min
Temperature	30°C
Detection	254 nm
Injection volume	15 µl
Pressure Drop	48 bars at 0.2 ml/min. System 12 bar.
Sample:	Certified diagnostic test 48270-U Supelco made of 4 parabens, methyl, ethyl, propyl, and butyl parabens.

Microbore column of 1 mm ID with a 50 cm length is an additional option for this type of media and can be run at 0.2 ml/min, a linear flow rate of > 1,500 cm/hr in using minute amounts of samples at pressures not exceeding 260 bars at such volumetric flow rates.



HPLC System.	Agilent 1290 with thermostatted column compartment and binary pump.
Columns	STYROS® 1R Simulated-Monolith™ 1 mm X 500 mm (0.392 ml volume)
Mobile phase.	A: 2 % ACN in H20, 0.1 % THF B: 100 % ACN, 0.1 % TFA
Flow rates	0.2 ml/min (> 1,500 cm/hr of linear velocity on an empty column)
Isocratic	40 % B for 20 min
Temperature	30°C
Detection	254 nm
Injection volume	20 µl
Pressure Drop	260 bars at 0.2 ml/min. System included.
Sample:	Certified diagnostic test 48270-U Supelco made of 4 parabens, methyl, ethyl, propyl, and butyl parabens.

The scientific community has sought, for some time without any success, to produce polystyrene divinyl benzene that does not disintegrate, leach, and contaminate the end products upon use.
Pharmacia as a subsidiary of Pfizer used polymerics as a final “polishing” step as their media was leaching.
The synthetic process is the old J Ugelstad emulsion method that consists of electrostatic passive connection of microsphere. Therefore, there is no active chemical bonding between microspheres that can easily fall apart.
It also relies on interstitial opening between beads with limitations including shear denaturing forces of biomolecules.
Their bulk processing media is the leaching agarose (Sepharose) based and in need of additional purifying euphemistically called “polishing” that seldom yields pure products and does not lend itself to automation.
The need for subzero temperatures is a clear indication of enzyme impurity that needs to be kept inactive by freezing to -70°C.
The process is slow as the dynamic capacities drop drastically compared to the static ones.
With low dynamic capacity, linear velocities need to be kept low, therefore extra-large columns with extra-large ID are used to impress and intimidate any observer at the scale of operation to be a challenge to match.
Any astute individual can assess instantly that such operation is not sustainable, should the requirement for production increase despite help from International Serum Institute of India.
As the responsible in charge have realized that we, in US, have made the proper decision to be able to rely on our domestic resources for tasks that involve our domestic health issues, especially in time of emergency, we need to look at any realistic option available to us.
The next move is for the FDA to increase the threshold of effectiveness from 50 % to a full 100 %.