NLAB SAGA™

SWEDISH EXCELLENCE IN NANOPORUS SILICA

NANOLOGICA

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CONTENT

NANOLOGICA'S VISION

"Better and cheaper medicine through porous silica"

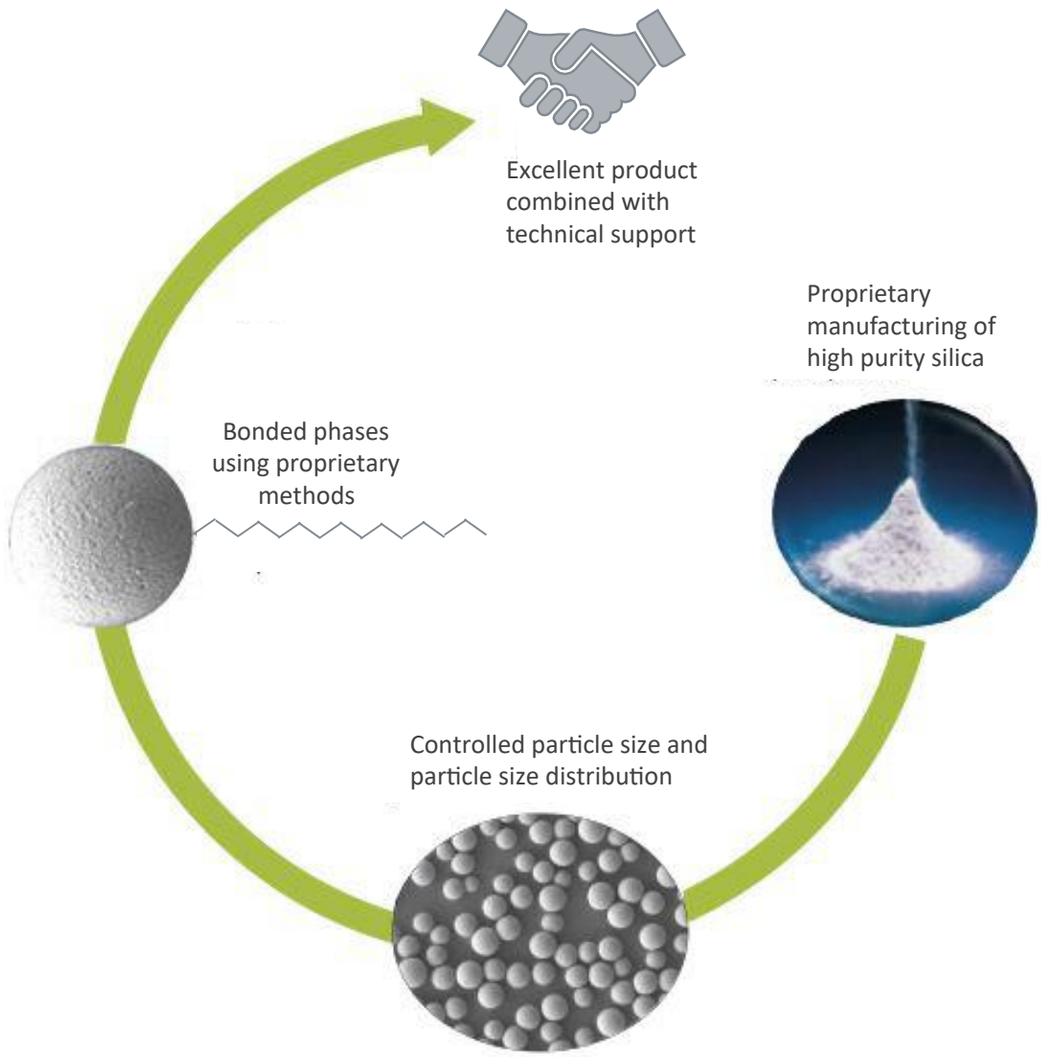
NLAB SAGA™

- Perfectly spherical, fully porous silica
- Tightly controlled particle size
- High purity silica- very low metal content
- High carbon content
- Exceptional chemical stability at high and low pH
- High loading

ABOUT NLAB SAGA™

Nanologica's core competency lies in developing nanoporous silica. NLAB Saga™ has been specifically developed to meet the expectations of industrial scale purification by chromatography. An optimized combination of pore volume, high surface area and high carbon load results in a robust and reliable product with stellar performance.

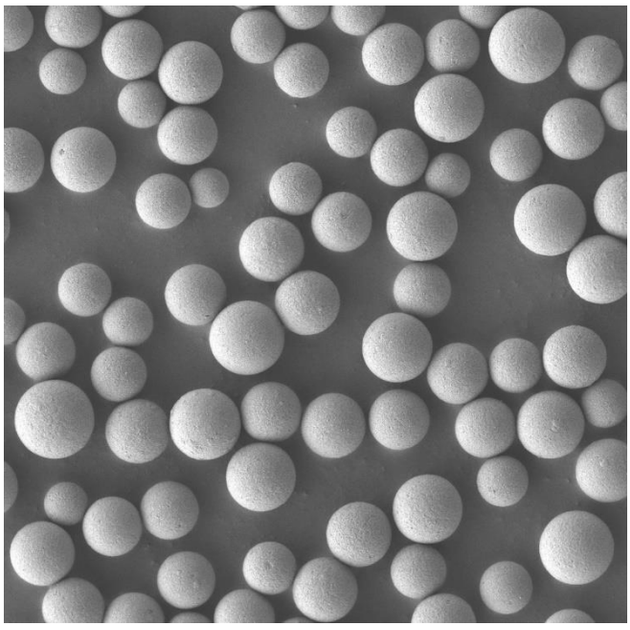
Nanologica has full control of the entire manufacturing process, from raw material to finished product. NLAB Saga™ has been tested and used by pharmaceutical companies worldwide manufacturing APIs at industrial scale where quality, performance and durability are uncompromisable.



NLAB SAGA™ PHYSICAL PROPERTIES

The large surface area and high pore volume combined with controlled particle size and distribution results in a silica with high loading capacity, high chemical stability and low backpressure, that is easy to pack. NLAB Saga™ is available in a variety of particles sizes from 10 to 15 µm.

- Surface area ~ 300 m^2/g
- Pore volume ~ 0.85 ml/g
- Pore size ~ 110 Å
- d90/d10 ≤1.7
- Low metal content
- Carbon load
  - C18 19%
  - C8 11%



High surface area

Pore volume 0.85 ml/g

Controlled particle size and distribution

High loading capacity

High mechanical stability

Easy to pack and low backpressure

CHEMICAL STABILITY

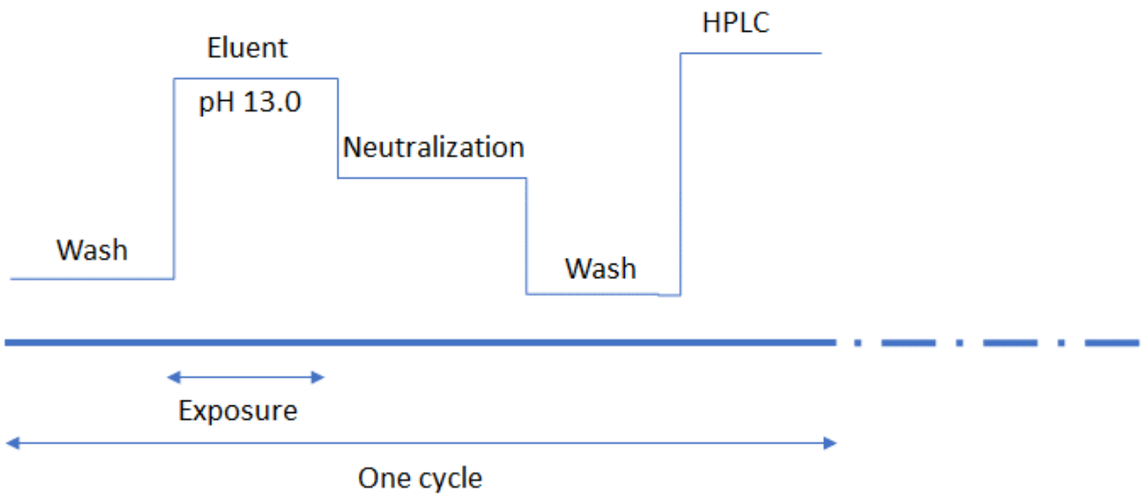
In large scale purification of proteins and peptides there will be depositions in the packing material. Toavoid time-consuming packing and unpacking of the columns it is important to run cleaning in process. These cleaning steps are usually performed at a very high pH. Such conditions are harsh for the silica, therefore it is of great importance that the silica survive under these conditions in order to have a long-lasting product.

Alkaline regeneration test designed to mimic wash cycles

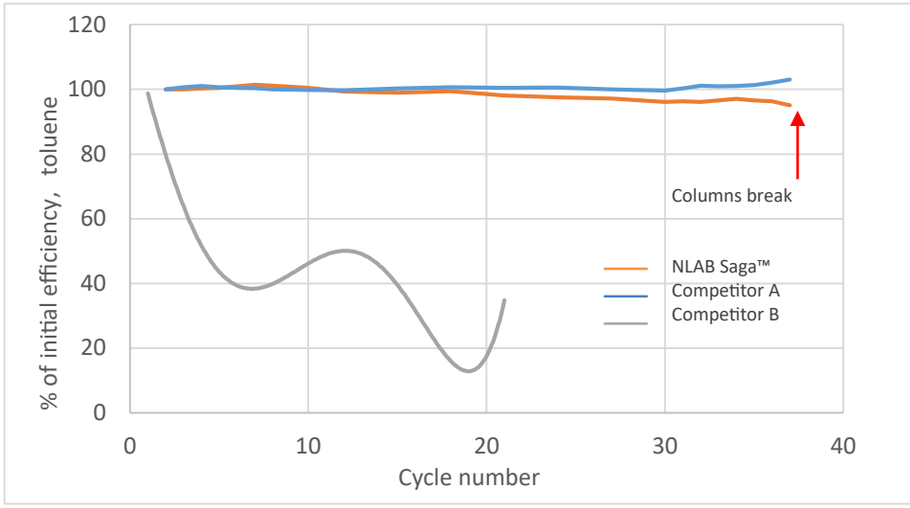
Test conditions:

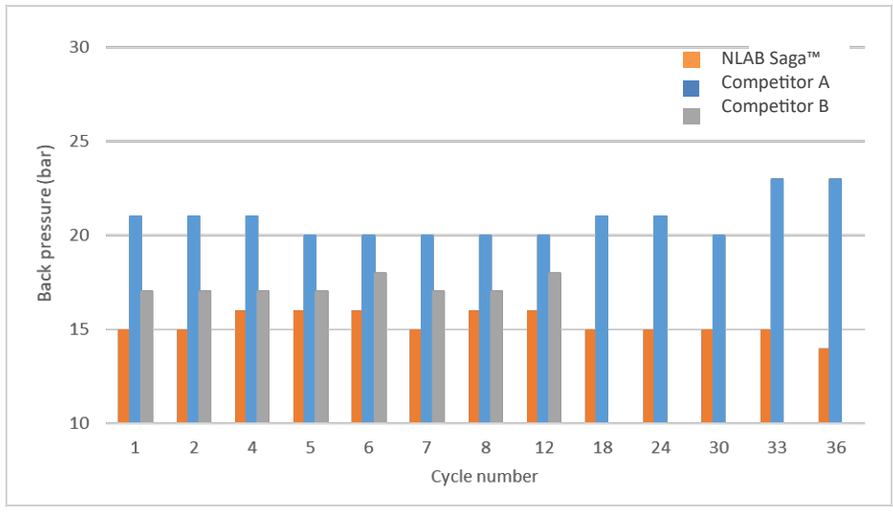
- Wash: 95/5 MeOH/H_2O, 10 CV
- Eluent: 60/40 MeOH/100mM NaOH, pH 13.0, 12 CV
- Temperature: Ambient cycle 1-30. From cycle 30 and onwards 50°C
- Neutralization: 90/10 MeOH/1%AcOH, 10CV
- Flow rate: 1ml/min
- Chromatographic evaluation

Illustration of one cycle



Comparison of NLAB Saga™ 13 µm C8, Competitor A 13 µm C8 and Competitor B 10 µm C8 in terms of alkaline stability shows that NLAB Saga™ and Competitor A performs consistently well and withstand the harsh experimental conditions, while Competitor B is falling behind.





<u>Chromatographic test conditions:</u>

Mobile phase: 80/20 MeOH/25 mM K-phosphate, pH 7.0

Flow rate: 1 ml/min

UV: 210 nm

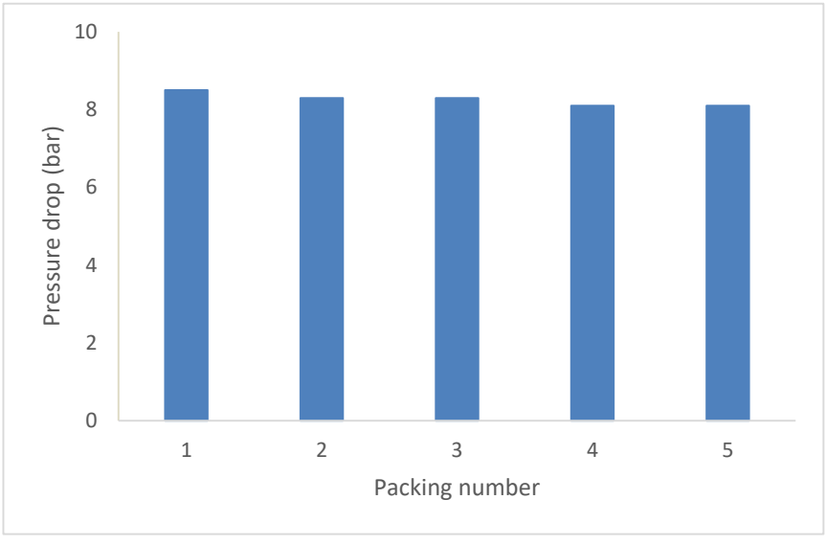
Temperature: 30°C, after 30 cycles the temperature was raised to <u>50°C</u> to speed up the experiment

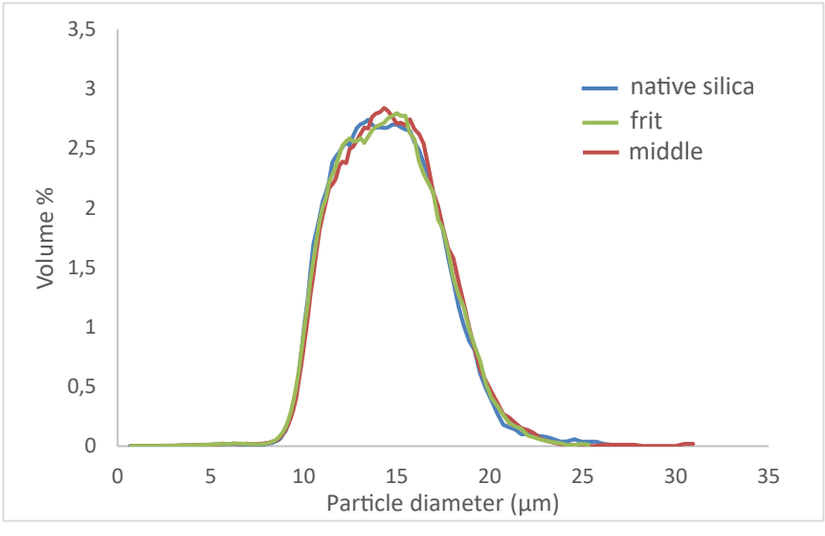
Analytes: Uracil, Toluene

Agilent 1100 system used for chromatographic evaluations and Schimadzu LC-20AD stand alone pump was used for regeneration simulation. The tests were performed at Nanologica's lab in Södertälje, Sweden.

MECHANICAL STABILITY

NLAB Saga™ has a high mechanical stability. Backpressure stays the same meaning there is no mechanical degradation of the silica. This is also shown by size distribution staying the same for native silica and used silica.



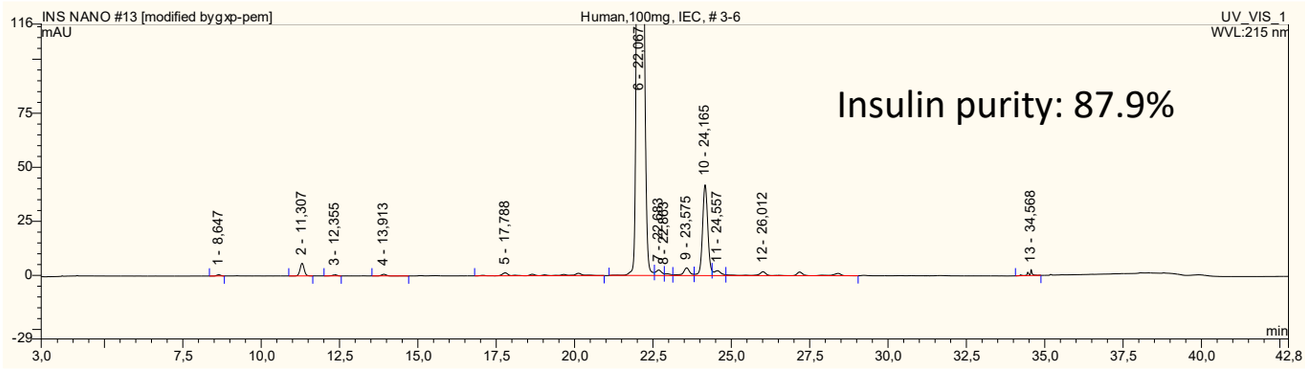


A DAC column with 5 cm internal diameter was used. 5 packings/unpackings to 100 bars were made with the same silica slurry.

EXAMPLE OF INSULIN PURIFICATION

The target for the experiment was to reach the purity threshold of 99.2% as set per the USP. Insulin purity was measured before and after one step of reversed-phase purification.

Insulin purity measured to 87.9% <u>BEFORE</u> reversed-phase purification



USP analytical method conditions

Flow rate:	1.2 ml/min
UV:	214 nm
Temperature:	40°C
Eluent:	A: 200mM Na_2SO_4/H_3PO_4 (pH=2.3)
	B: Acetonitrile/ 200mM Na_2SO_4/H_3PO_4 (pH=2.3) 45/55
Gradient:	0-30 min / 57%B; 30-44 min /57-89%B; 44-50 min / 89%B

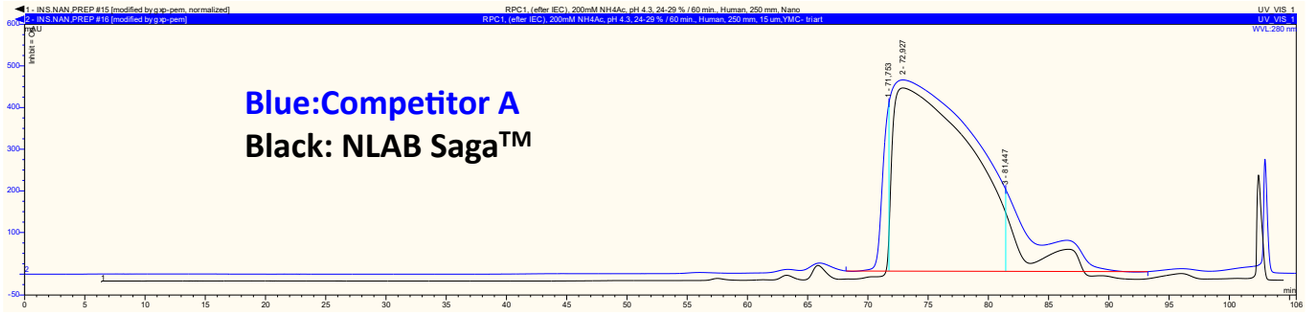
Experimental set up

The mass overload experiments were performed under the same conditions for NLAB Saga™ and the competitor.

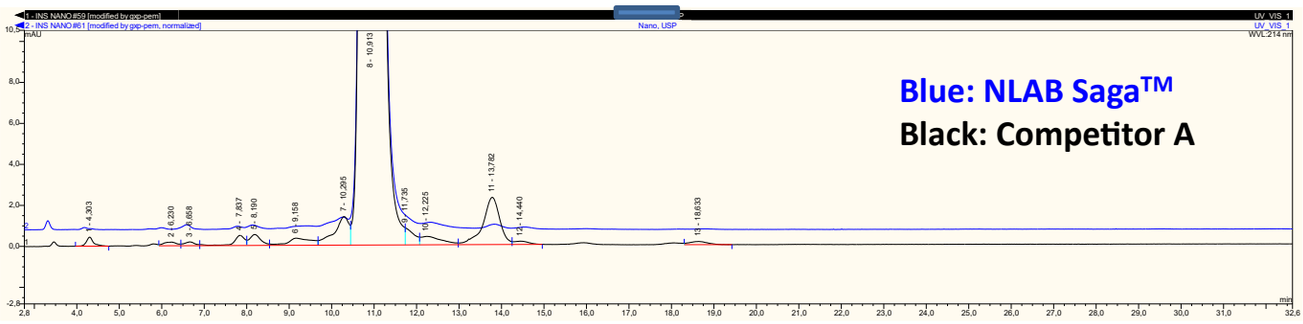
Process parameters which were kept constant:

- **Loading**: 0.37 g/cm^2 column crossectional area (15 g/ liter)
- **Yield**: 90 % ± 1 % in all steps
- **Slope of the gradient:** (0.083 % / minute, pH= 4.3)
- **Linear flow rate**: 180 cm/h
- **Organic solvent**: Acetonitrile
- **Feed**: Insulin with 87.9 % purity

Mass overload -
the exact same fraction from the insulin purification for both Competitor A and NLAB Saga™



Insulin purity measured to 99.5% <u>AFTER</u> one step of reversed-phase purification



Company	Phase	USP method Purity (%)	Backpressure * (Bar)
Nanologica	NLAB Saga™ C8	99.50	15.5
Competitor A	C8	97.08	10.2
Competitor B	C8	98.56	19.8
Competitor C	C8	98.82	21.5

NLAB Saga™ surpasses the set USP target by reaching a purity of 99.5% after one step of reversed-phase purification. The Competitors A, B and C do not reach the USP target, meaning they would need one more step of purification to pass the USP threshold.

Thus, NLAB Saga™ needs fewer steps to reach the USP purity target leading to a lower manufacturing cost for the insulin manufacturer.

NOTES

CONTACT DETAILS AND ORDER INFORMATION

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