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Author: Porta, Fabiola
Title: Mesoporous silica nanoparticles as drug delivery systems
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General method for MSNs synthesis

All reagents and solvents were commercial products purchased from Sigma-aldrich Chemie B. V. or Biosolve B. V. and used as received. TLC analysis was conducted on TLC-plastic sheets 60 F_{254} (Merck) with detection of UV absorbtion with a Camag lamp. Milli-Q water with resistance of more than 18.2 MΩ/cm was provided by a Millipore Milli-Q filtering system with filtration trough a 0.22 μm Millipak filter. Silica cromatography purifications have been done with Silica Gel, with particle size 40-63 μm and pore size 60 Å, purchased by Screening devices B. V.

FT-IR spectra were acquired with a BIORAD Excalibur Series FTS 4000 instrument, dispersing in dry 200 mg of KBr 2 mg of synthesized material and pressing the powders with a Graseby Specac powder presser, with a pressure of 13 tons.

^{1}H-NMR spectra were measured with a Bruker AV-400 (400 MHz), and chemical shitfs are reported in ppm downfield from internal tetramethylsilane (0.00 ppm). Abbreviations used are s=singlet, d=doublet, dd=doublet of doublets, m=multiplet, br=broad.

TEM was conducted on a JEOL 1010 instrument with an accelerating voltage of 60 kV. Samples for TEM were prepared by placing a drop of each solution on carbon-coated copper grids. After ~ 10 minutes the droplet was removed from the edge of the grid. UV-VIS absorbance spectra were obtained with a PerkinElmer precisely Lambda 25 UV-VIS spectrometer. The particle shape was analyzed with a NovaSEM microscope. Flow cytometry was performed with a Beckham Coulter Cell Lab Quanta SC. Confocal laser scanning microscopy (CLSM) was performed using a Carl Zeiss Observer, LSM 5 exciter.

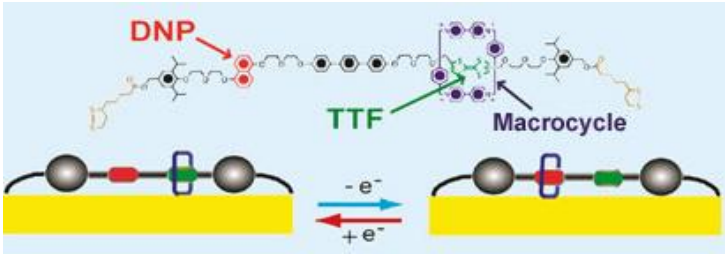
Synthesis of Mesoporous Silica Nanoparticles. In a flask 2g Hexadecyltrimethyl-ammonium bromide (CTAB), was dissolved in 960 ml of Milli-Q water and 7 ml of 2N NaOH. The solution was heated at 80 °C for 30 min and 9 g of TEOS was added. After two hours, filtration of the reaction mixture yielded a white solid with a yield of 58%.

The surfactant was removed from the particles (5.2g) by refluxing overnight in a mixture of methanol (310 ml) and fuming hydrochloric acid 37% (31 ml) under an inert atmosphere. Filtration resulted in a white powder with a yield of 60%. The removal of CTAB from the silica particles was confirmed using FT-IR.

Glossary

Rotaxane:

is a mechanically-interlocked molecular architecture consisting of a "dumbbell shaped molecule" which is threaded through a "macrocycle" as represented below.



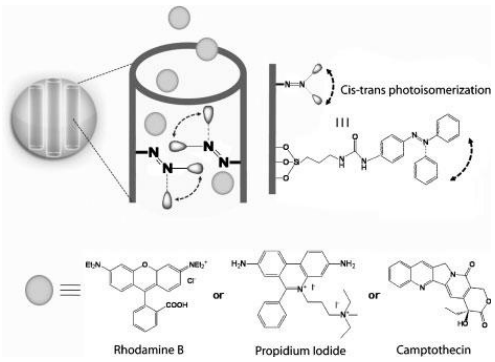
The macrocycle associates with one dumbshell molecule or the other depending on the environment conditions. One of the two dumbshell is tetrathiafulvalene (TTF) which attracts the macrocycle in neutral conditions, and repels it in reducing conditions. This molecular machine has been studied by the group of Prof. Stoddart of Northwestern University in Illinois.

Nanovalve:

is an evolution of the rotaxane concept. The rotaxane is a molecular machine however in the nanovalve one of the two dumbshell molecules is the mesoporous silica nanoparticles itself.

Nanoimpeller:

is molecular machine which switches from a *cis* to a *trans* conformation depending of the irradiating wavelength. Nanoimpellers were studied by the group of Prof. Zink in UCLA and were used to functionalize the internal surface of mesoporous silica nanoparticles as represent in the following cartoon.



List of Publications

Cyclodextrin/dextran Based Drug Carriers for a Controlled Release of Hydrophobic Drugs in Zebrafish Embryos, Ke Peng, Chao Cui, Itsuro Tomatsu, **Fabiola Porta**, Annemarie H. Meijer, Herman P. Spaink and Alexander Kros, *Soft Matter*, **2010**, 6, 3778-3783

Peptide Modified Mesoporous Silica Nanocontainers, **Fabiola Porta**, Gerda E.M. Lamers, Jeffrey I. Zink and Alexander Kros, *PCCP*, **2011**, 13, 9982-9985

Mesoporous Silica Nanoparticles as a Compound Delivery System in Zebrafish Embryos, Faiza Sharif, **Fabiola Porta**, Annemarie H. Meijer, Alexander Kros and Michael Richardson, *Int. J. of Nanomedicine*, manuscript accepted

PEG-Modified Mesoporous Silica Nanoparticles for Delivery of Hydrophobic Drugs in Xenopus Laevis, **Fabiola Porta**, Nabila Bardine, Gerda E. M. Lamers, Antony Durston and Alexander Kros, *MolPharm*, manuscript submitted

Folic Acid Modified Mesoporous Silica Nanoparticles for Cellular and Nuclear Targetd Drug Delivery, **Fabiola Porta**, Gerda E. M. Lamers, Jess Morrhayim, Antonia Chatzopoulou, Marcel Schaaf, Hans den Dulk, Claude Backendorf, Jeffrey I. Zink, and Alexander Kros, manuscript in preparation

Colloidosomes as Implantable Beads for the in vivo Delivery of Hydorphobic Drugs, **Fabiola Porta** and Alexander Kros, manuscript in preparation

In vivo Evaluation of PEG-coated Mesoporous Silica Nanoparticles as Drug Delivery Systems of Hydorphobic Drugs, **Fabiola Porta**, Nabila Bardine, Antony Druston and Alexander Kros, manuscript in preparation

Selected presentations

In vivo evaluation of modified mesoporous nanoparticles, **Fabiola Porta** and Alexander Kros, NWO Netherlands Organization for Scientific Research, Selected lecture, 2011

Silica mesoporous nanoparticles versatile tools for drug delivery, **Fabiola Porta** and Alexander Kros, European Materials Research Society, 2011

Curriculum Vitae

Fabiola Porta was born in Milano on the 25th of March 1982. After completing her secondary education at Liceo Scientifico Vittorio Veneto in Milano, she started her academic study in Pharmacy (Chimica e Tecnologia Farmaceutica) at Università degli studi, Milano, in 2001. She graduated in February 2008 with a thesis concerning the synthesis of quinoline-derivates as antimalarial drugs with Prof. Sergio Romeo. In March 2008 she began her PhD career at Leiden University in the Soft Chemistry Matter under the supervision of Prof. Dr. Ir. J. G. E. M. Fraaije and Dr. Alexander Kros. During her PhD project she collaborated with several groups to understand and establish the role of mesoporous silica nanoparticles as drug delivery systems. Fruitful collaborations were started with Dr. Claude Backendorf, Dr. Nabila Bardine and Prof. Antony Durston. In December 2009 she attended the Article 9 course at Leiden University Medical Center in order to study the *in vivo* release of compounds from Pickering stabilized microparticles.
After the completion of her PhD she plans to continue in this field of research.