

Nanohydrogel Formation within the Halloysite Lumen for Triggered and Sustained Release

Parisi F., Evtugyn V., Rozhina E., Fakhrullin R.
Kazan Federal University, 420008, Kremlevskaya 18, Kazan, Russia

Abstract

© 2018 American Chemical Society. An easy strategy to obtain nanohydrogels within the halloysite nanotube (HNTs) lumen was investigated. Inorganic reverse micelles based on HNTs and hexadecyltrimethylammonium bromides were dispersed in chloroform, and the hydrophilic cavity was used as a nanoreactor to confine the gel formation based on alginate cross-linked by calcium ions. Spectroscopy and electron microscopy experiments proved the confinement of the polymer into the HNT lumen and the formation of calcium-mediated networks. Biological tests proved the biocompatibility of the hybrid hydrogel. The nanogel in HNTs was suitable for drug loading and sustained release with the opportunity of triggered burst release by chemical stimuli. Here, we propose a new strategy based on inorganic reverse micelles for nanohydrogel formation, which are suitable for industrial and biological applications as well as for selective and triggered adsorption and/or release.

<http://dx.doi.org/10.1021/acsami.7b19361>

References

- [1] Ganguly, K.; Chaturvedi, K.; More, U. A.; Nadagouda, M. N.; Aminabhavi, T. M. Polysaccharide-Based Micro/Nanohydrogels for Delivering Macromolecular Therapeutics. *J. Controlled Release* 2014, 193, 162-173, 10.1016/j.jconrel.2014.05.014
- [2] Eastoe, J.; Hollamby, M. J.; Hudson, L. Recent Advances in Nanoparticle Synthesis with Reversed Micelles. *Adv. Colloid Interface Sci.* 2006, 128-130, 5-15, 10.1016/j.cis.2006.11.009
- [3] Pileni, M.-P. The Role of Soft Colloidal Templates in Controlling the Size and Shape of Inorganic Nanocrystals. *Nat. Mater.* 2003, 2, 145-150, 10.1038/nmat817
- [4] Sahiner, N.; Godbey, W. T.; McPherson, G. L.; John, V. T. Microgel, Nanogel and Hydrogel-hydrogel Semi-IPN Composites for Biomedical Applications: Synthesis and Characterization. *Colloid Polym. Sci.* 2006, 284, 1121-1129, 10.1007/s00396-006-1489-4
- [5] Zhou, X.; Yang, Q.; Li, J.; Nie, J.; Tang, G.; Du, B. Thermo-Sensitive Poly(VCL-4VP-NVP) Ionic Microgels: Synthesis, Cytotoxicity, Hemocompatibility, and Sustained Release of Anti-Inflammatory Drugs. *Mater. Chem. Front.* 2017, 1, 369-379, 10.1039/c6qm00046k
- [6] Ghugare, S. V.; Mozetic, P.; Paradossi, G. Temperature-Sensitive Poly(Vinyl Alcohol)/Poly(Methacrylate-Co-N-Isopropyl Acrylamide) Microgels for Doxorubicin Delivery. *Biomacromolecules* 2009, 10, 1589-1596, 10.1021/bm900185u
- [7] Yang, Q.; Wang, K.; Nie, J.; Du, B.; Tang, G. Poly(N-Vinylpyrrolidone) Microgels: Preparation, Biocompatibility, and Potential Application as Drug Carriers. *Biomacromolecules* 2014, 15, 2285-2293, 10.1021/bm5004493
- [8] Cassano, R.; Trombino, S.; Ferrarelli, T.; Barone, E.; Arena, V.; Mancuso, C.; Picci, N. Synthesis, Characterization, and Anti-Inflammatory Activity of Diclofenac-Bound Cotton Fibers. *Biomacromolecules* 2010, 11, 1716-1720, 10.1021/bm100404q
- [9] Dadsetan, M.; Taylor, K. E.; Yong, C.; Bajzer, Ž.; Lu, L.; Yaszemski, M. J. Controlled Release of Doxorubicin from PH-Responsive Microgels. *Acta Biomater.* 2013, 9, 5438-5446, 10.1016/j.actbio.2012.09.019

- [10] Liu, K.-H.; Liu, T.-Y.; Chen, S.-Y.; Liu, D.-M. Drug Release Behavior of Chitosan-montmorillonite Nanocomposite Hydrogels Following Electrostimulation. *Acta Biomater.* 2008, 4, 1038-1045, 10.1016/j.actbio.2008.01.012
- [11] Lvov, Y.; Wang, W.; Zhang, L.; Fakhrullin, R. Halloysite Clay Nanotubes for Loading and Sustained Release of Functional Compounds. *Adv. Mater.* 2016, 28, 1227-1250, 10.1002/adma.201502341
- [12] Kryuchkova, M.; Danilushkina, A.; Lvov, Y.; Fakhrullin, R. Evaluation of Toxicity of Nanoclays and Graphene Oxide in Vivo: A Paramecium Caudatum Study. *Environ. Sci.: Nano* 2016, 3, 442-452, 10.1039/c5en00201j
- [13] Vergaro, V.; Abdullayev, E.; Lvov, Y. M.; Zeitoun, A.; Cingolani, R.; Rinaldi, R.; Leporatti, S. Cytocompatibility and Uptake of Halloysite Clay Nanotubes. *Biomacromolecules* 2010, 11, 820-826, 10.1021/bm9014446
- [14] Fakhrullina, G. I.; Akhatova, F. S.; Lvov, Y. M.; Fakhrullin, R. F. Toxicity of Halloysite Clay Nanotubes in Vivo: A Caenorhabditis Elegans Study. *Environ. Sci.: Nano* 2015, 2, 54-59, 10.1039/c4en00135d
- [15] Zhao, Y.; Abdullayev, E.; Vasiliev, A.; Lvov, Y. Halloysite Nanotubule Clay for Efficient Water Purification. *J. Colloid Interface Sci.* 2013, 406, 121-129, 10.1016/j.jcis.2013.05.072
- [16] Cavallaro, G.; Lazzara, G.; Milioto, S.; Parisi, F.; Sanzillo, V. Modified Halloysite Nanotubes: Nanoarchitectures for Enhancing the Capture of Oils from Vapor and Liquid Phases. *ACS Appl. Mater. Interfaces* 2014, 6, 606-612, 10.1021/am404693r
- [17] Luo, P.; Zhang, J.-s.; Zhang, B.; Wang, J.-h.; Zhao, Y.-f.; Liu, J.-d. Preparation and Characterization of Silane Coupling Agent Modified Halloysite for Cr(VI) Removal. *Ind. Eng. Chem. Res.* 2011, 50, 10246-10252, 10.1021/ie200951n
- [18] Zhao, M.; Liu, P. Adsorption Behavior of Methylene Blue on Halloysite Nanotubes. *Microporous Mesoporous Mater.* 2008, 112, 419-424, 10.1016/j.micromeso.2007.10.018
- [19] Lvov, Y.; Abdullayev, E. Functional Polymer-clay Nanotube Composites with Sustained Release of Chemical Agents. *Prog. Polym. Sci.* 2013, 38, 1690-1719, 10.1016/j.progpolymsci.2013.05.009
- [20] Abdullayev, E.; Sakakibara, K.; Okamoto, K.; Wei, W.; Ariga, K.; Lvov, Y. Natural Tubule Clay Template Synthesis of Silver Nanorods for Antibacterial Composite Coating. *ACS Appl. Mater. Interfaces* 2011, 3, 4040-4046, 10.1021/am200896d
- [21] Barrientos-Ramírez, S.; Ramos-Fernández, E. V.; Silvestre-Albero, J.; Sepúlveda-Escribano, A.; Pastor-Blas, M. M.; González-Montiel, A. Use of Nanotubes of Natural Halloysite as Catalyst Support in the Atom Transfer Radical Polymerization of Methyl Methacrylate. *Microporous Mesoporous Mater.* 2009, 120, 132-140, 10.1016/j.micromeso.2008.08.015
- [22] Wang, R.; Jiang, G.; Ding, Y.; Wang, Y.; Sun, X.; Wang, X.; Chen, W. Photocatalytic Activity of Heterostructures Based on TiO₂ and Halloysite Nanotubes. *ACS Appl. Mater. Interfaces* 2011, 3, 4154-4158, 10.1021/am201020q
- [23] Cavallaro, G.; Donato, D. I.; Lazzara, G.; Milioto, S. Films of Halloysite Nanotubes Sandwiched between Two Layers of Biopolymer: From the Morphology to the Dielectric, Thermal, Transparency, and Wettability Properties. *J. Phys. Chem. C* 2011, 115, 20491-20498, 10.1021/jp207261r
- [24] Gorrasi, G.; Pantani, R.; Murariu, M.; Dubois, P. PLA/Halloysite Nanocomposite Films: Water Vapor Barrier Properties and Specific Key Characteristics. *Macromol. Mater. Eng.* 2014, 299, 104-115, 10.1002/mame.201200424
- [25] De Silva, R. T.; Pasbakhsh, P.; Goh, K. L.; Chai, S.-P.; Ismail, H. Physico-Chemical Characterisation of Chitosan/Halloysite Composite Membranes. *Polym. Test.* 2013, 32, 265-271, 10.1016/j.polymertesting.2012.11.006
- [26] He, Y.; Kong, W.; Wang, W.; Liu, T.; Liu, Y.; Gong, Q.; Gao, J. Modified Natural Halloysite/Potato Starch Composite Films. *Carbohydr. Polym.* 2012, 87, 2706-2711, 10.1016/j.carbpol.2011.11.057
- [27] Liu, M.; Wu, C.; Jiao, Y.; Xiong, S.; Zhou, C. Chitosan-Halloysite Nanotubes Nanocomposite Scaffolds for Tissue Engineering. *J. Mater. Chem. B* 2013, 1, 2078-2089, 10.1039/c3tb20084a
- [28] Lee, Y.; Jung, G.-E.; Cho, S. J.; Geckeler, K. E.; Fuchs, H. Cellular Interactions of Doxorubicin-Loaded DNA-Modified Halloysite Nanotubes. *Nanoscale* 2013, 5, 8577-8585, 10.1039/c3nr02665e
- [29] Yang, J.; Wu, Y.; Shen, Y.; Zhou, C.; Li, Y.-F.; He, R.-R.; Liu, M. Enhanced Therapeutic Efficacy of Doxorubicin for Breast Cancer Using Chitosan Oligosaccharide-Modified Halloysite Nanotubes. *ACS Appl. Mater. Interfaces* 2016, 8, 26578-26590, 10.1021/acsami.6b09074
- [30] Massaro, M.; Lazzara, G.; Milioto, S.; Noto, R.; Riela, S. Covalently Modified Halloysite Clay Nanotubes: Synthesis, Properties, Biological and Medical Applications. *J. Mater. Chem. B* 2017, 5, 2867-2882, 10.1039/c7tb00316a
- [31] Lvov, Y. M.; Shchukin, D. G.; Möhwald, H.; Price, R. R. Halloysite Clay Nanotubes for Controlled Release of Protective Agents. *ACS Nano* 2008, 2, 814-820, 10.1021/nn800259q
- [32] Joussein, E.; Petit, S.; Churchman, J.; Theng, B.; Righi, D.; Delvaux, B. Halloysite Clay Minerals-a Review. *Clay Miner.* 2005, 40, 383-426, 10.1180/0009855054040180
- [33] Pasbakhsh, P.; Churchman, G. J.; Keeling, J. L. Characterisation of Properties of Various Halloysites Relevant to Their Use as Nanotubes and Microfibre Fillers. *Appl. Clay Sci.* 2013, 74, 47-57, 10.1016/j.clay.2012.06.014

- [34] Luo, Z.; Song, H.; Feng, X.; Run, M.; Cui, H.; Wu, L.; Gao, J.; Wang, Z. Liquid Crystalline Phase Behavior and Sol-Gel Transition in Aqueous Halloysite Nanotube Dispersions. *Langmuir* 2013, 29, 12358-12366, 10.1021/la402836d
- [35] Liu, M.; He, R.; Yang, J.; Zhao, W.; Zhou, C. Stripe-like Clay Nanotubes Patterns in Glass Capillary Tubes for Capture of Tumor Cells. *ACS Appl. Mater. Interfaces* 2016, 8, 7709-7719, 10.1021/acsami.6b01342
- [36] Bertolino, V.; Cavallaro, G.; Lazzara, G.; Milioto, S.; Parisi, F. Biopolymer-Targeted Adsorption onto Halloysite Nanotubes in Aqueous Media. *Langmuir* 2017, 33, 3317-3323, 10.1021/acs.langmuir.7b00600
- [37] Cavallaro, G.; Lazzara, G.; Milioto, S. Exploiting the Colloidal Stability and Solubilization Ability of Clay Nanotubes/Ionic Surfactant Hybrid Nanomaterials. *J. Phys. Chem. C* 2012, 116, 21932-21938, 10.1021/jp307961q
- [38] Cavallaro, G.; Lazzara, G.; Milioto, S.; Palmisano, G.; Parisi, F. Halloysite Nanotube with Fluorinated Lumen: Non-Foaming Nanocontainer for Storage and Controlled Release of Oxygen in Aqueous Media. *J. Colloid Interface Sci.* 2014, 417, 66-71, 10.1016/j.jcis.2013.11.026
- [39] Cavallaro, G.; Grillo, I.; Gradzielski, M.; Lazzara, G. Structure of Hybrid Materials Based on Halloysite Nanotubes Filled with Anionic Surfactants. *J. Phys. Chem. C* 2016, 120, 13492-13502, 10.1021/acs.jpcc.6b01282
- [40] Owoseni, O.; Nyankson, E.; Zhang, Y.; Adams, S. J.; He, J.; McPherson, G. L.; Bose, A.; Gupta, R. B.; John, V. T. Release of Surfactant Cargo from Interfacially-Active Halloysite Clay Nanotubes for Oil Spill Remediation. *Langmuir* 2014, 30, 13533-13541, 10.1021/la503687b
- [41] Yah, W. O.; Takahara, A.; Lvov, Y. M. Selective Modification of Halloysite Lumen with Octadecylphosphonic Acid: New Inorganic Tubular Micelle. *J. Am. Chem. Soc.* 2012, 134, 1853-1859, 10.1021/ja210258y
- [42] Cavallaro, G.; Lazzara, G.; Milioto, S.; Parisi, F. Hydrophobically Modified Halloysite Nanotubes as Reverse Micelles for Water-in-Oil Emulsion. *Langmuir* 2015, 31, 7472-7478, 10.1021/acs.langmuir.5b01181
- [43] Cavallaro, G.; Danilushkina, A.; Evtugyn, V.; Lazzara, G.; Milioto, S.; Parisi, F.; Rozhina, E.; Fakhrullin, R. Halloysite Nanotubes: Controlled Access and Release by Smart Gates. *Nanomaterials* 2017, 7, 199, 10.3390/nano7080199
- [44] Dzamukova, M. R.; Naumenko, E. A.; Lvov, Y. M.; Fakhrullin, R. F. Enzyme-Activated Intracellular Drug Delivery with Tubule Clay Nanoformulation. *Sci. Rep.* 2015, 5, 10560, 10.1038/srep10560
- [45] Mackie, A.; Bajka, B.; Rigby, N. Roles for Dietary Fibre in the Upper GI Tract: The Importance of Viscosity. *Food Res. Int.* 2016, 88, 234-238, 10.1016/j.foodres.2015.11.011
- [46] Cavallaro, G.; Lazzara, G.; Milioto, S. Dispersions of Nanoclays of Different Shapes into Aqueous and Solid Biopolymeric Matrices. Extended Physicochemical Study. *Langmuir* 2011, 27, 1158-1167, 10.1021/la103487a
- [47] Sidheswaran, P.; Bhat, A. N.; Ganguli, P. Intercalation of Salts of Fatty Acids Into Kaolinite. *Clays Clay Miner.* 1990, 38, 29-32, 10.1346/ccmn.1990.0380104
- [48] Sartori, C.; Finch, D. S.; Ralph, B.; Gilding, K. Determination of the Cation Content of Alginate Thin Films by FTIR Spectroscopy. *Polymer* 1997, 38, 43-51, 10.1016/s0032-3861(96)00458-2
- [49] Arık, M.; Çelebi, N.; Onganer, Y. Fluorescence Quenching of Fluorescein with Molecular Oxygen in Solution. *J. Photochem. Photobiol., A* 2005, 170, 105-111, 10.1016/j.jphotochem.2004.07.004
- [50] Vinokurov, V. A.; Stavitskaya, A. V.; Chudakov, Y. A.; Ivanov, E. V.; Shrestha, L. K.; Ariga, K.; Darrat, Y. A.; Lvov, Y. M. Formation of Metal Clusters in Halloysite Clay Nanotubes. *Sci. Technol. Adv. Mater.* 2017, 18, 147-151, 10.1080/14686996.2016.1278352
- [51] Gombotz, W. R.; Wee, S. Protein Release from Alginate Matrices. *Adv. Drug Delivery Rev.* 1998, 31, 267-285, 10.1016/s0169-409x(97)00124-5
- [52] Ritger, P. L.; Peppas, N. A. A Simple Equation for Description of Solute Release I. Fickian and Non-Fickian Release from Non-Swellable Devices in the Form of Slabs, Spheres, Cylinders or Discs. *J. Controlled Release* 1987, 5, 23-36, 10.1016/0168-3659(87)90034-4
- [53] Makaremi, M.; Pasbakhsh, P.; Cavallaro, G.; Lazzara, G.; Aw, Y. K.; Lee, S. M.; Milioto, S. Effect of Morphology and Size of Halloysite Nanotubes on Functional Pectin Bionanocomposites for Food Packaging Applications. *ACS Appl. Mater. Interfaces* 2017, 9, 17476-17488, 10.1021/acsami.7b04297