

Sweet Nanomaterials: Carbohydrate-Coated Carbon Nanotubes and Glyconanosomes as Advanced Nanovectors for Drug Delivery.

Juan-José Cid¹, Mohyeddin Assali¹, Manuel Pernía-Leal¹, Inmaculada Fernández², Miguel Muñoz³, Ralf Wellinger³ and Nouredine Khier^{1*}

¹Grupo de Química Bioorgánica, Instituto de Investigaciones Químicas (IIQ), C.S.I.C. and Universidad de Sevilla. C/ Américo Vespucio 49, 41092, Seville, Spain. ²Departamento de Química Orgánica y Farmacéutica, Universidad de Sevilla. C/ Profesor García González 2, 41012 Seville, Spain. ³Centro Andaluz de Biología Molecular y Medicina Regenerativa (CABIMER), 41092 Seville, Spain.

khier@iiq.csic.es

Single-walled carbon nanotubes (SWCNTs)¹ have received an unrivalled interest as consequence of their unique structural, mechanical, electrical, and optical properties that make them promising candidates for biomedical applications.^{2,3} To overcome their inherent insolubility in biological media various approximations, including covalent and non-covalent functionalization, have been developed. Nevertheless, these methods suffer from important drawbacks such as the low stability of the obtained aggregates or the disruption of π -electronic character of the CNTs sidewalls. In order to solve these problems, we have recently reported a *bottom-up* approach based on the supramolecular self-organization of diacetylenic-based glycolipids on the SWCNTs sidewalls, followed by photopolymerization to form polydiacetylene glycolipid-coated nanotubes.⁴⁻⁷ By using this methodology, the resulting nano-assemblies are water soluble, highly stable and show a biomimetic and multivalent presentation of carbohydrates on their surface, and besides, without altering the physico-chemical properties of the inner tube.⁷

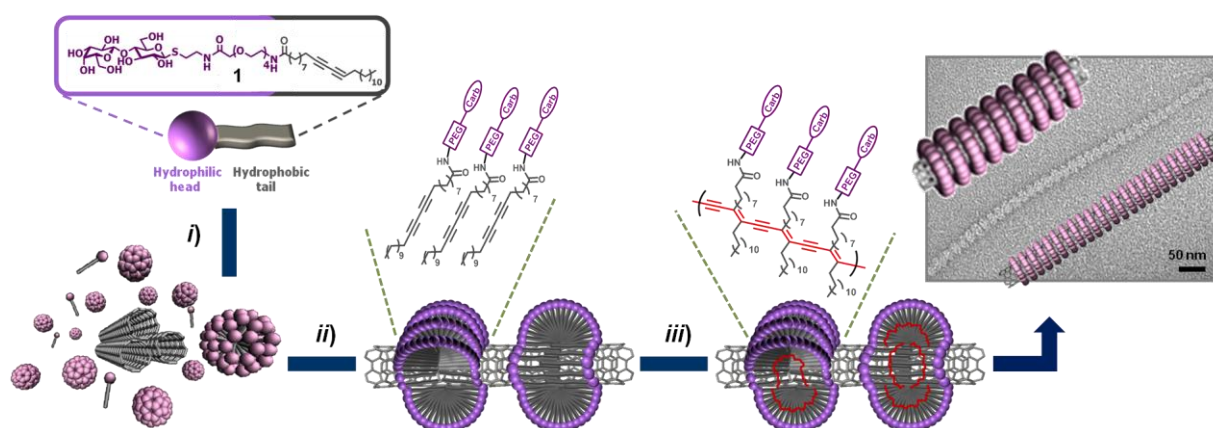


Figure 1. Supramolecular self-assembly and photopolymerization of diacetylenic-based glycolipid **1** on the nanotube surface, and TEM characterization showing the abacus-like topology of the nanoconstructs.

In the present communication, we are aimed at discussing: a) the synthesis and characterization of glyconanoring-coated SWCNTs with **1**-type glycolipids (Figure 1), b) their selective binding to lectins (Figure 2A) and their specific aggregation of uropathogenic *Escherichia coli* bacteria (Figure 2B), and c) the glyconanoring sliding out of the carbon nanotubes to afford a new class of disk-shaped amphiphilic biomaterials named *glyconanosomes* (GNSs) (Figure 3).

Hence, the ability of GNSs to encapsulate lipophilic molecules will be presented, together with comparative results of *in vitro* activity of their inclusion complex with camptothecin (CPT) (GNS/CPT) as nanoparticle-based drug delivery systems of 3rd generation for the controlled delivery of CPT in the inhibition of carcinogenic cell proliferation.⁸

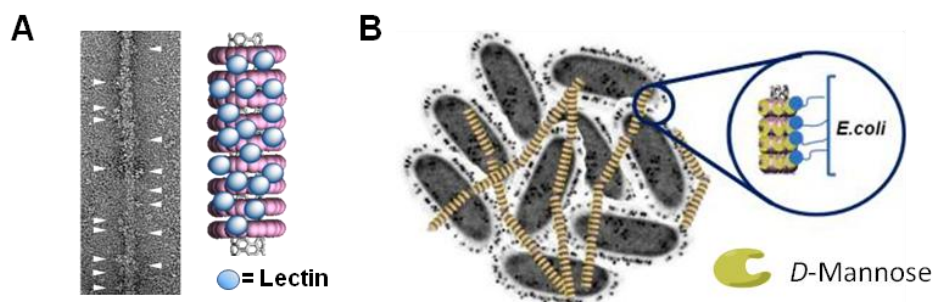


Figure 2. Specific interaction of SWCNT/glycolipids with lectins, and application in the selective aggregation of uropathogenic bacteria.

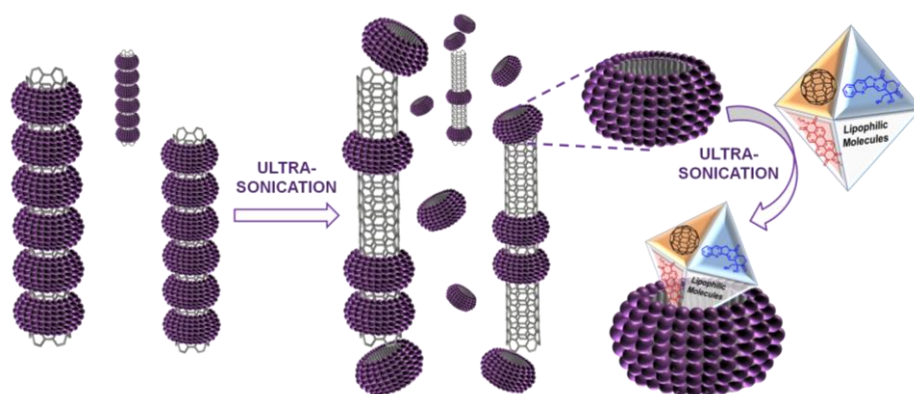


Figure 3. Synthesis of glyconanosomes (GNSs) by the ultra-sonication-induced sliding out method and application in the water solubilization of the hydrophobic C_{60} , perylene-bisimide and the cytotoxic camptothecin (CPT).

References

- [1] Iijima, S., *Nature*, **354** (1991) 56.
- [2] X. Chen, A. Kis, A. Zettl, C.R. Bertozzi, *Proc. Natl. Acad. Sci. U.S.A.*, **20** (2007) 8218.
- [3] Z. Liu, C. Davis, W. Cai, X. Chen, H.J. Dai, *Proc. Natl. Acad. Sci. U.S.A.*, **5** (2008) 1410.
- [4] M. Assali, M. Pernía-Leal, I. Fernández, R. Baati, C. Mioskowski, N. Khiar, *Soft Matter*, **5** (2009) 948.
- [5] N. Khiar, M. Pernía-Leal, R. Baati, C. Ruhlmann, C. Mioskowski, P. Schultz, I. Fernández, *Chem. Commun.* **27** (2009) 4121.
- [6] M. Assali, M. Pernía Leal, I. Fernández, R. Baati, N. Khiar, *Nano Res.*, **11** (2010) 764.
- [7] M. Pernía Leal, M. Assali, I. Fernández, N. Khiar, *Chem. Eur. J.*, **6** (2011) 1828.
- [8] M. Assali, J.-J. Cid, M. Pernía-Leal, M. Muñoz-Bravo, I. Fernández, R. E. Wellinger, N. Khiar, *ACS Nano*, **3** (2013) ASAP (DOI: 10.1021/nn304986x).