Efficient MW promoted Synthesis of Cyclodextrin-grafted Nanomaterials: three examples of nanoscale multicarriers

Katia Martina, Giancarlo Cravotto, Marina Caporaso, Emanuela Calcio Gaudino, Francesca Baricco and Gloria Berlier.

Dipartimento di Scienza e Tecnologia del Farmaco, University of Turin, Italy; katia.martina@unito.it

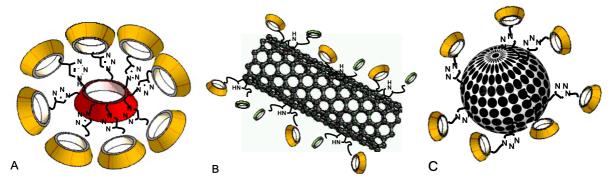
The development of alternative template molecules as efficient carriers is still very much a work in progress. An ideal vehicle requires specific structural features: a highly functionalized surface, the propensity to self-order and predictable and reproducible pharmacokinetics (PK) and pharmacodynamics (PD). Functionalized nanoparticles that allow molecular recognition of the target tissue have been widely used for active or triggered delivery of drugs. Unfortunately, the key design parameters that govern the performance of nanocarriers and liposomes suffer from a lack of preparative reproducibility.

Notably, MW irradiation promote efficient and selective modification of the CD surface and MW-promoted 1,3-dipolar cycloaddition can be exploited for the synthesis of CD based multicarrier.¹⁻³ Here we present the preparation of three new vehicles: a new water soluble oligocyclodextrin heterononamer (A),⁴ a new hybrid SWCNTs platform that bind β -CD units as well as DOTA (B),⁵ and highly functionalized β -CD-grafted mesoporous silica (C).

Two efficient synthetic approaches based on MW promoted Cu-catalyzed 1,3dipolar cycloaddition (CuAAC) between CD monoazides and alkynyl moieties as well as 1,3-dipolar cycloaddition of *in situ* generated azomethine ylides will be described.

The CD grafted SWCNTs and the CD-derivatized silica have been fully characterized by means of different techniques. Thanks to non-conventional synthetic protocols under microwave and ultrasound irradiation we could obtain clean and highly derivatized nanomaterials. Moreover their negligible toxicity do not affect cell viability.

The *in silico* prediction of the loading ratio of the oligomeric nanostructure and the relaxometric titration to assess their potential as contrast agents for MRI diagnostics; confirmed their potential for pharmaceutical and diagnostic applications.



- 1. Tagliapietra S.; Cravotto G.; Calcio Gaudino E.; Visentin S.; Mussi V. Synlett, 2012, 23, 1459-1462
- Cintas P.; Martina, K. Robaldo, B. Garella, A. Boffa, L. Cravotto, G. Collect. Czech. Chem. Commun. 2007, 72, 1014-1024
- 3. Cravotto G.; Fokin V.; Garella D.; Binello A.; L. Boffa, and A. Barge, J. Comb. Chem., 2010, 12, 13-15.
- 4. Barge, A.; Caporaso, M.; Cravotto, G.; Martina, K.; Tosco, P.; Aime, S.; Carrera, C.; Gianolio, E.; Pariani, G.; Corpillo, D. *Chemistry Eur. J.*, 2013, 19, 12086-12092
- 5. Calcio Gaudino E.; Tagliapietra S.; Martina K.; Barge A.; Lolli M.; Terreno E.; Lembo D.; Cravotto, G. submitted