Hybrid Polylactic Acid (PLA) / Mesostructured Cellular Foam (MCF) Silicate Carriers for the Encapsulation and Controlled Release of Water Insoluble Drugs

Dimitris Giliopoulos, Evi Christodoulou, Dimitris Bikiaris and Konstantinos Triantafyllidis

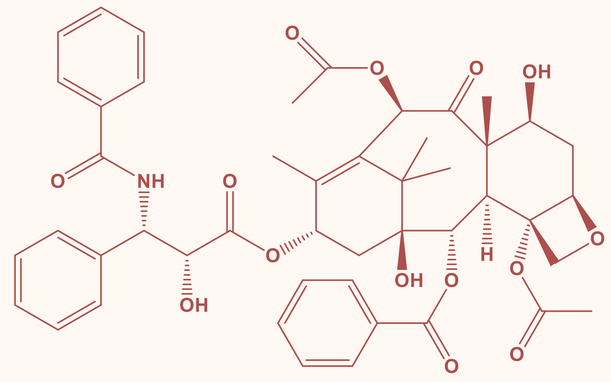
Department of Chemistry, Aristotle University of Thessaloniki

Introduction

- Two major problems correlated with the usage of hydrophobic drugs are: i) the difficult delivery in the aqueous environment of human cells and ii) the limitation of organic solvents that can be used in industry
- Delivery of hydrophobic substances inside human cells can be facilitated by using mesoporous silicas as carriers
- MCF silicas are mesoporous particles with large pore sizes and siliceous walls full of surface hydroxyl groups, that have foam-like morphology and can be organically functionalized
- PLA is a biodegradable polyester that is widely used in drug delivery applications, either as standalone carrier or as a component of more complex systems
- Paclitaxel (PTX) is a highly hydrophobic substance, that is used as chemotherapy medication to treat a number of types of cancer. PTX is given by injection into a vein

Scope of the present study

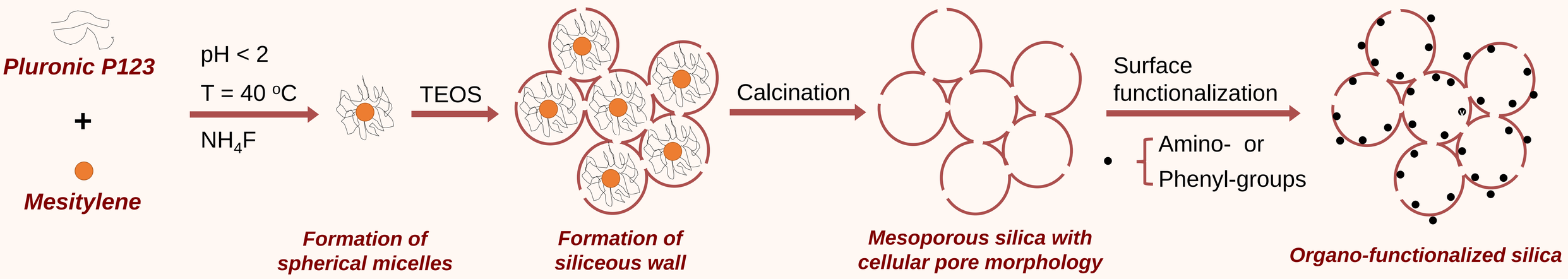
Absorption of PTX into pristine an organically modified MCF, formation of hybrid carrier systems with PLA and study of the drug release profiles



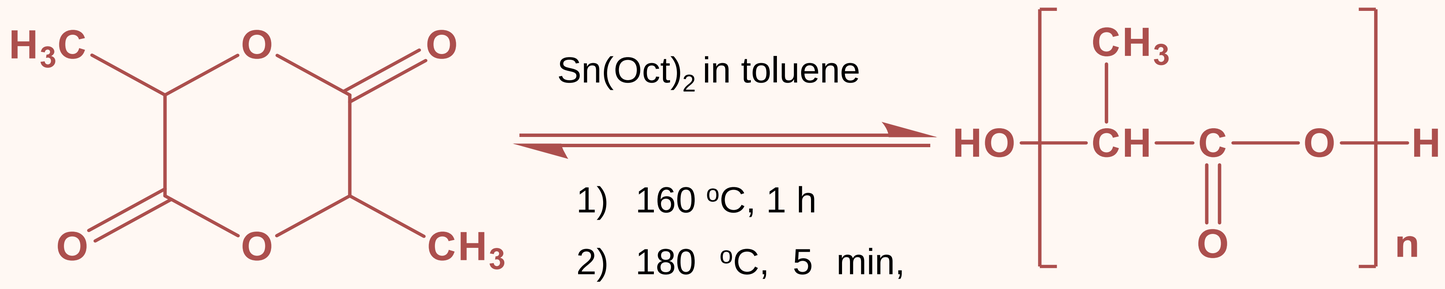
Paclitaxel (PTX)

Experimental

MCF synthesis and organic functionalization



PLA synthesis



Lactide ***PLA***

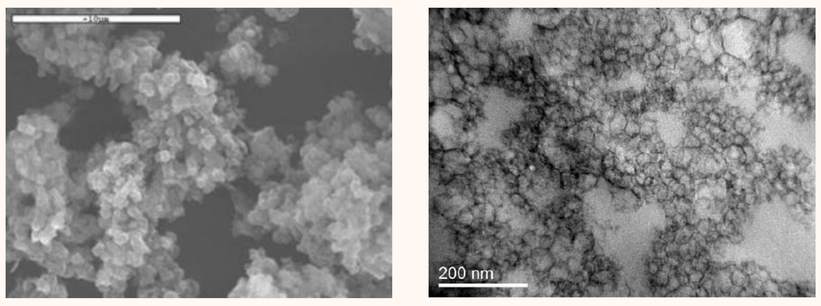
Production of PLA/MCF carriers

Hybrid carriers via water/oil emulsion

- MCF dispersion in PVA aqueous solution
- PLA dilution in chloroform
- Mixing and homogenization (TURAX) of the two parts
- Solvent evaporation
- Hybrid carriers separation
- Freeze drying

Results

MCF morphology & structure



SEM ***TEM***

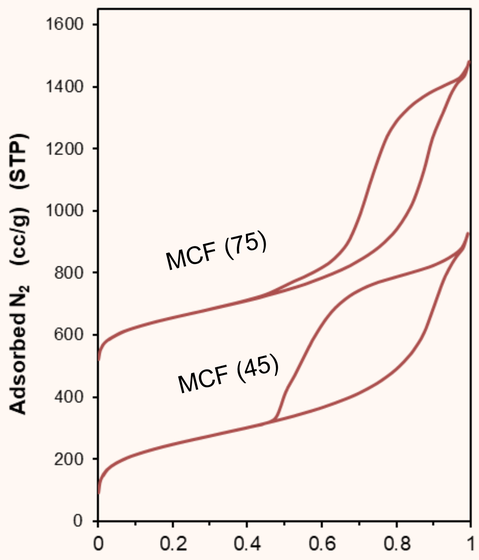
- MCF with foam-like morphology and primary particles of irregular shape (tending to spherical)
- Spherical cells (pores) with large diameters and narrow windows. Good uniformity

Carbon analysis of organo-MCF

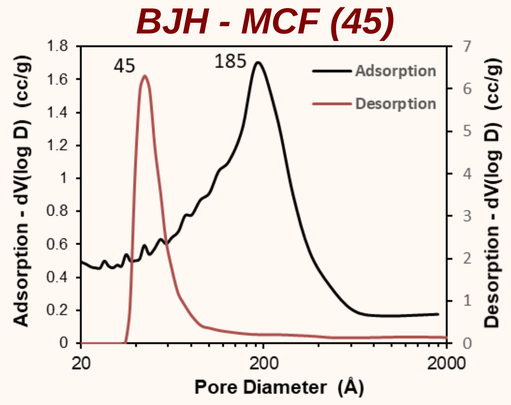
Sample	Carbon content (wt %)
MCF with phenyl-groups	18.4
MCF with amino-groups	7.2

N_2 adsorption of pristine MCFs

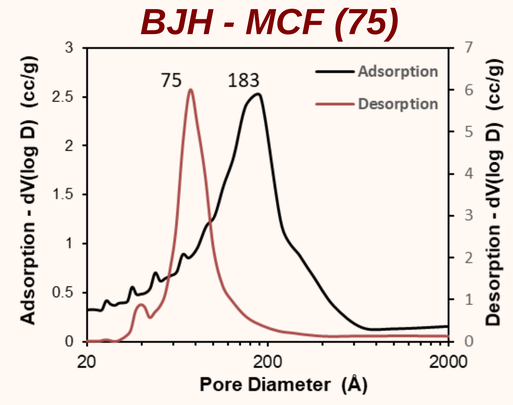
Isotherms



BJH - MCF (45)



BJH - MCF (75)

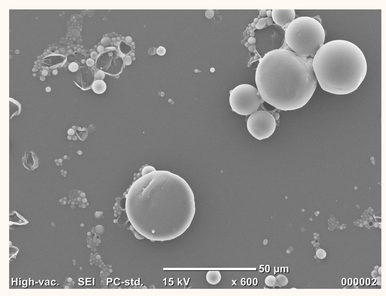


Sample	Surface Area (m^2/g)	Tot. Pore Vol. (cc/g)	Pore Size Ad. (Å)	Pore Size De. (Å)
MCF (45)	895	1.432	185	45
MCF (75)	747	1.592	183	75

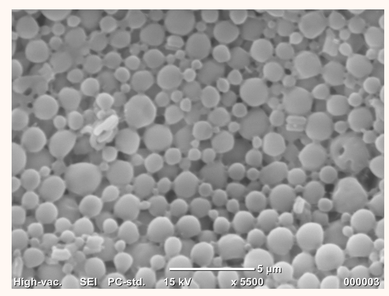
PLA characterization

Physical Properties of PLA	
Specific Gravity	1.24
Relative Viscosity	2.5
Crystalline Melt Temperature (°C)	155 – 170
Glass Trantition Temperature (°C)	55 – 60
Clarity	Transparent

Hybrid PLA/MCF carriers



SEM – PLA



SEM – PLA/MCF

Concluding Remarks – Future work

- Effective synthesis of pristine and organically modified MCF silicas with various structural and morphological characteristics, that are able to absorb the hydrophilic drug Paclitaxel
- Effective synthesis of PLA with high Mw, that can be used for the production of hybrid PLA/MCF carriers via emulsion/solvent evaporation method
- Study of the PTX absorption kinetics in correlation with the different MCF pore sizes and surface functional groups
- Testing of different techniques to produce PLA/MCF carriers (e.g. melt mixing)

Acknowledgements - Funding

ΕΣΠΑ 2014-2020 ανάπτυξη - εργασία - αλληλεγγύη

Πράξη: «Ενίσχυση μεταδιδακτόρων ερευνητών/ερευνητριών (MIS: 5001552)

Τίτλος έρευνας: «Ενθυλάκωση της δραστικής ουσίας Paclitaxel σε υβριδικούς φορείς πορωδών νανο- και μικρο-σωματιδίων/ βιοαποικοδομήσιμων αλειφατικών πολυεστέρων και μελέτη του ρυθμού αποδέσμευσης αυτής»

ΙΔΡΥΜΑ ΚΡΑΤΙΚΩΝ ΥΠΟΤΡΟΦΙΩΝ ΙΚΥ