

Nanogels for pulmonary drug delivery

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PuDeRegels -
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• INTRODUCTION •

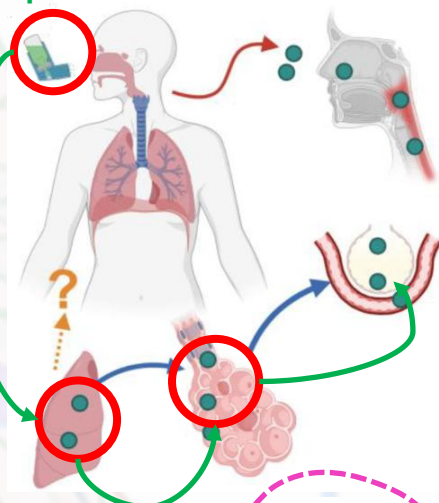
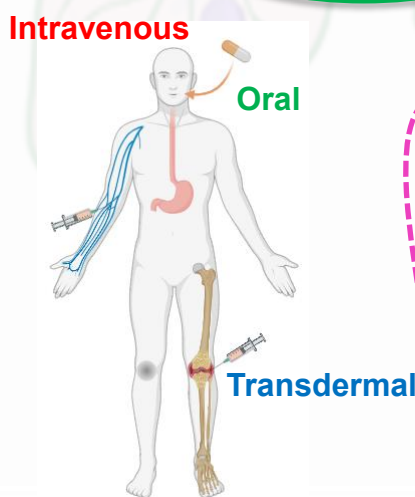
- Research for cancer
- New strategies for delivering drugs and new therapies
- Cancer is still one of the leading cause of death globally according WHO
- Breast cancer and lung cancer are the two most frequent type of cancers

Scope: Synthesis-preparation of microgels (MG) with the incorporation of smart NGs for pulmonary delivery of an anticancer drug to the lungs. The nanocarrier system will have a targeting moiety for cancer cells and stealth ability for better incorporating the nanogel into the deep lung.

Ideal formulation

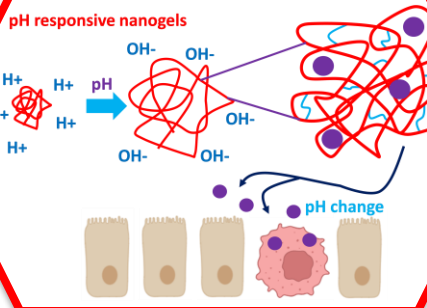
- Avoid of respiratory tract defence mechanisms
- Macrophages
- Mucoadhesive
- Ideal size for lung 0.5-5 μm

pH responsiveness to cancer cells

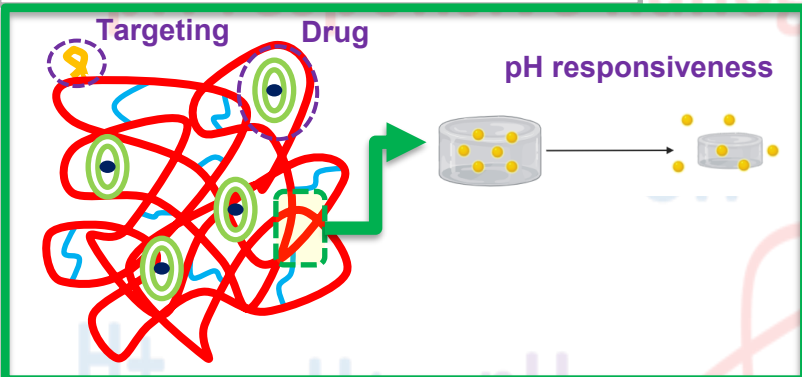
Introduction Dispersion
Targeting

Why?

- High surface area
- Local and systemic treatment
- Reduction of systemic side effects
- Reduction of higher doses of the drug at the site of action of the drug



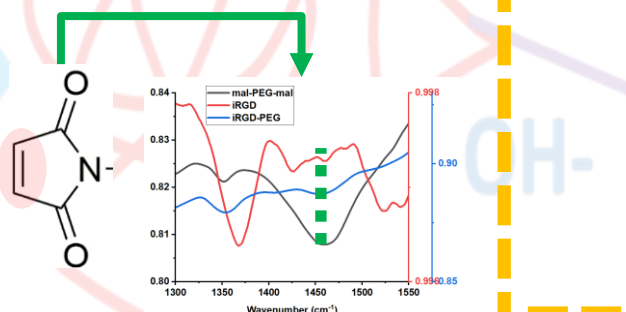
• RESULTS •



Encapsulation

- Drug solubility in water 8-12%
- pH affects solubility
- Different analogies γ -Cyclodextrin:drug
- Water:ethanol mixtures
- Maximum encapsulation around 40-50%

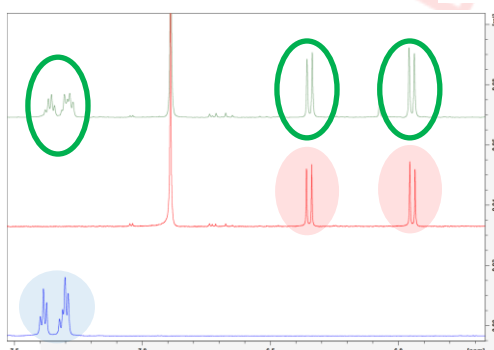
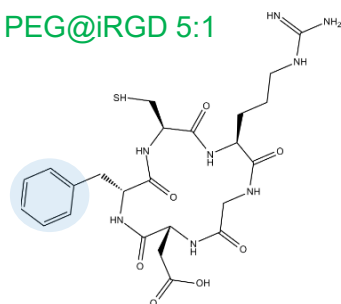
Conjugation of iRGD with PEG-mal-2



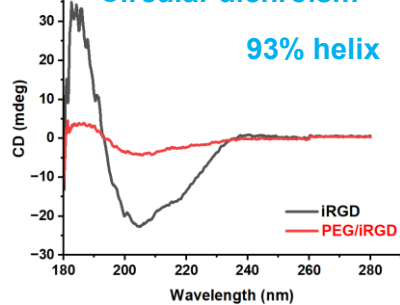
Objectives

- Drug encapsulation
- Bioconjugation (PEG-iRGD)
- pH-responsive nanogels
- Nanogels-in-microgels

PEG@iRGD 5:1



Circular dichroism



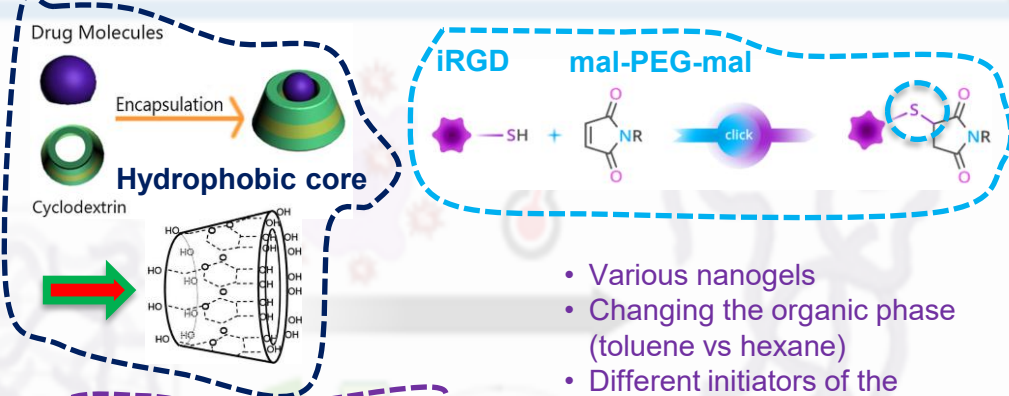
• CONCLUSIONS •

- Increased encapsulation of the drug in the cyclodextrin
- Bioconjugation of the targeting moiety with the crosslinker
- pH responsiveness from 6.7 to 7.4 for various nanogels
- Introduce flow cytometry in characterization for the responsiveness

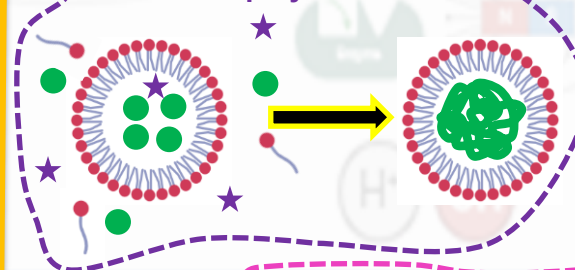
• EXPERIMENTAL •

Entrectinib: selective tyrosine kinase inhibitor with specificity, at low nanomolar concentrations

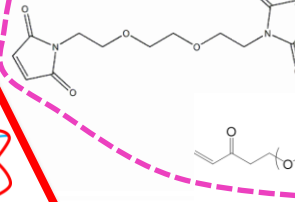
iRGD peptide: increase accumulation and penetration of anticancer drugs into tumours, but not into normal tissues



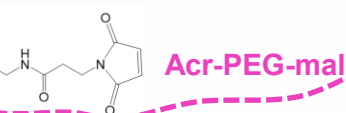
Emulsion polymerization



PEG-mal-2



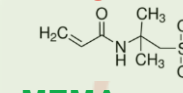
PEG-mal-4



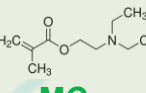
Acr-PEG-mal



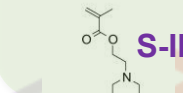
AMPS



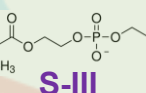
DEAEMA



MEMA



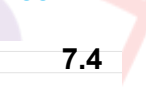
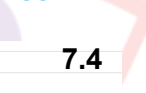
MC



S-I



S-II



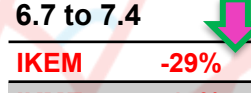
Change of surfactant tween



Change of composition



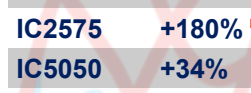
pH changes from 6.7 to 7.4



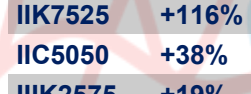
pH 6.7



pH 7.4



pH 6.9



pH 6.7



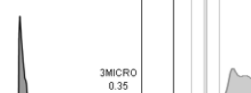
pH 7.4



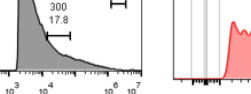
pH 6.7



pH 7.4



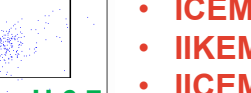
pH 6.7



pH 7.4



pH 6.7



pH 7.4



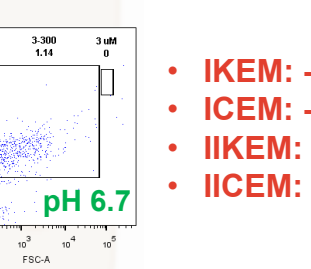
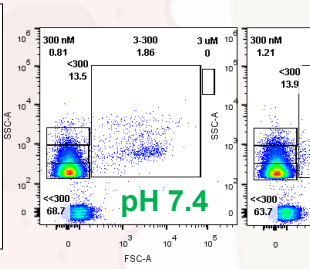
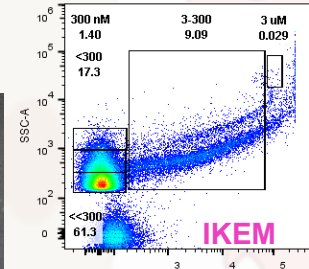
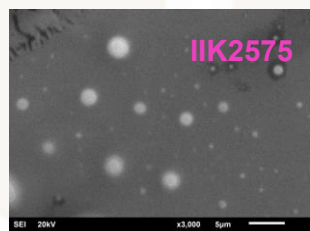
- IKEM: -28%
- ICEM: -20%
- IIKEM: +5%
- IIICEM: -25%

References:

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- Flow cytometry Unit
- NMR Unit



300-3000 nm