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Formulation of ferrocifens loaded nanocapsules against multidrug resistant ovarian adenocarcinoma



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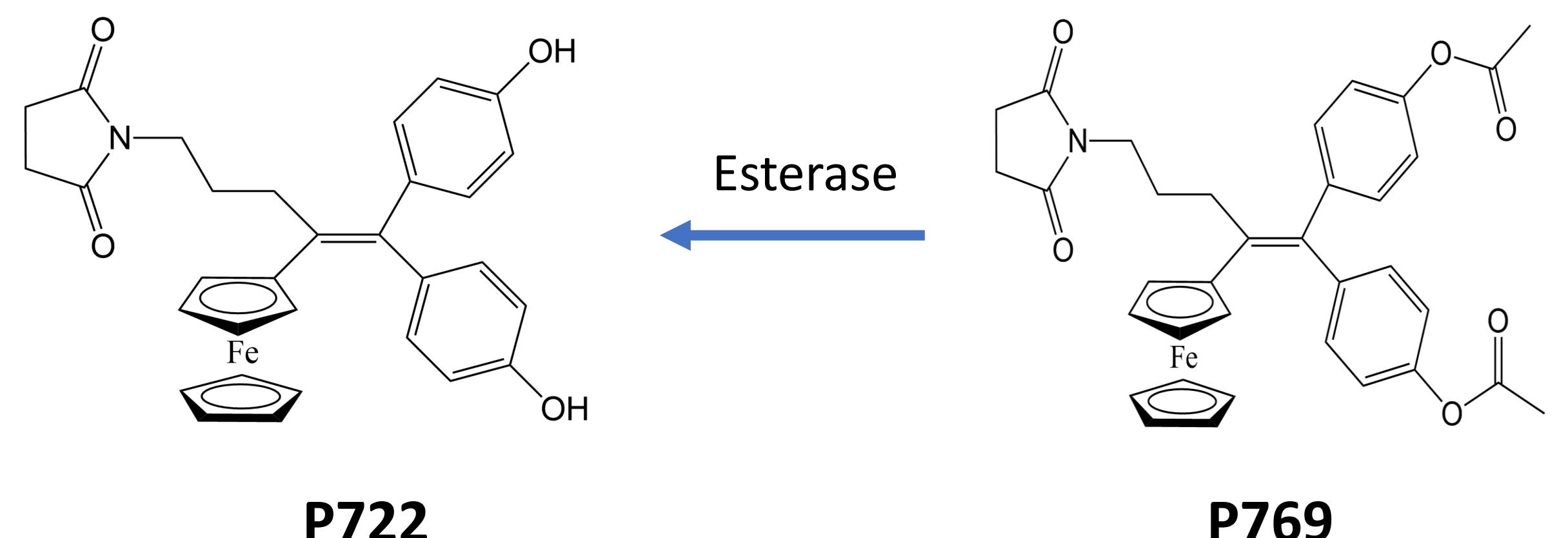
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Introduction

Considering that ovarian adenocarcinoma is one of the deadliest epithelial malignancies in women, owing to the resistance of the current treatments, new strategies are needed [1]. P722 and P769 are innovative organometallic complexes, named ferrocifens, and could be an alternative. P722 is the most efficient ferrocifen on several cancer cell lines such as ovarian cancer [2]. However, these molecules are strongly lipophilic. Therefore, in order to be administered *in vivo*, there is a need to use nanocarriers, as lipid nanocapsules (LNC) [3]. The aim of this project is to formulate the corresponding ferrocifen loaded LNC in order to reach specifically the ovarian adenocarcinoma, by incorporating on the LNC surface a cell-penetrating peptide, TLS [4] which targets the SKOV3 ovarian cancer cell lines.

Ferrocifens mechanism of action

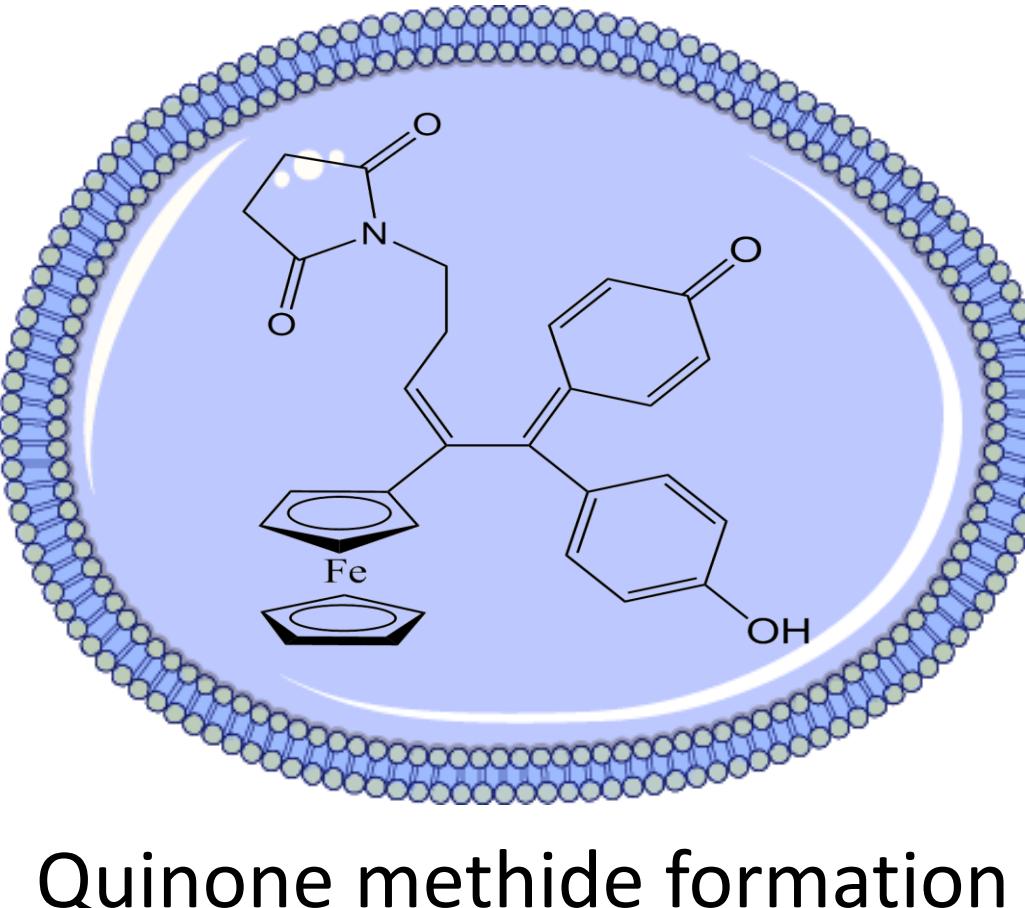


P722

P769

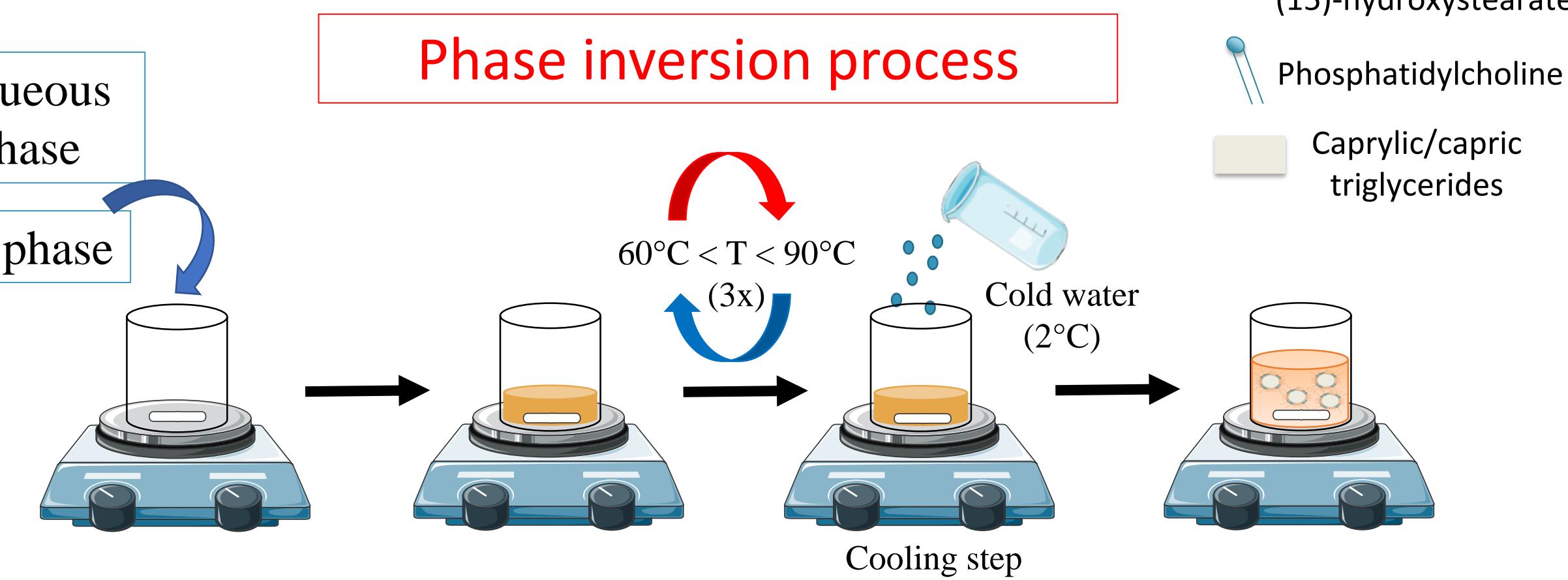
	IC ₅₀		
Compounds	A2780	A2780-Cis	SKOV3
P722	0,035 µM	0,049 µM	0,30 µM
Carboplatin	1,2 µM	11,5 µM	23,8 µM

Lipophilic

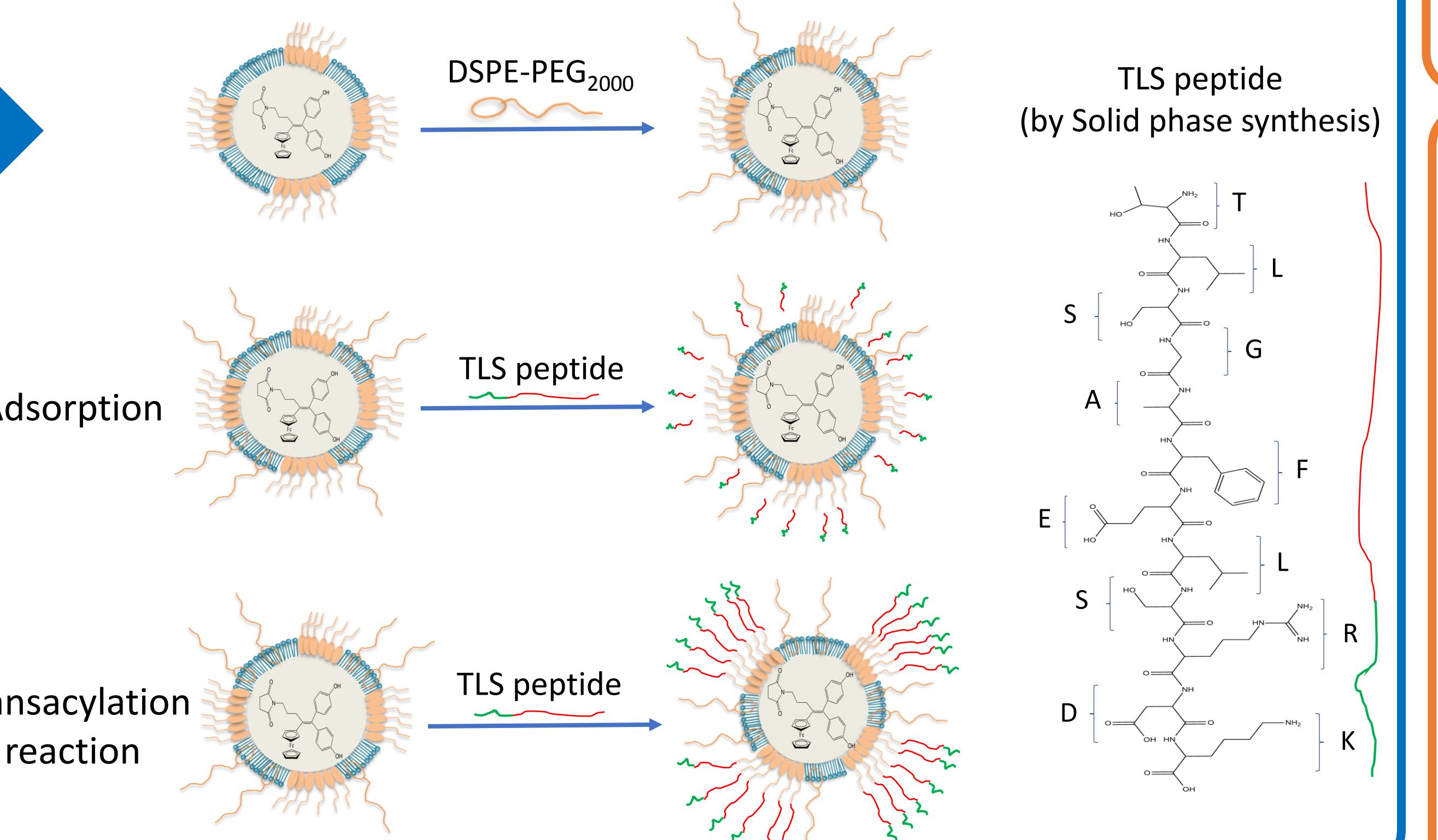


Quinone methide formation

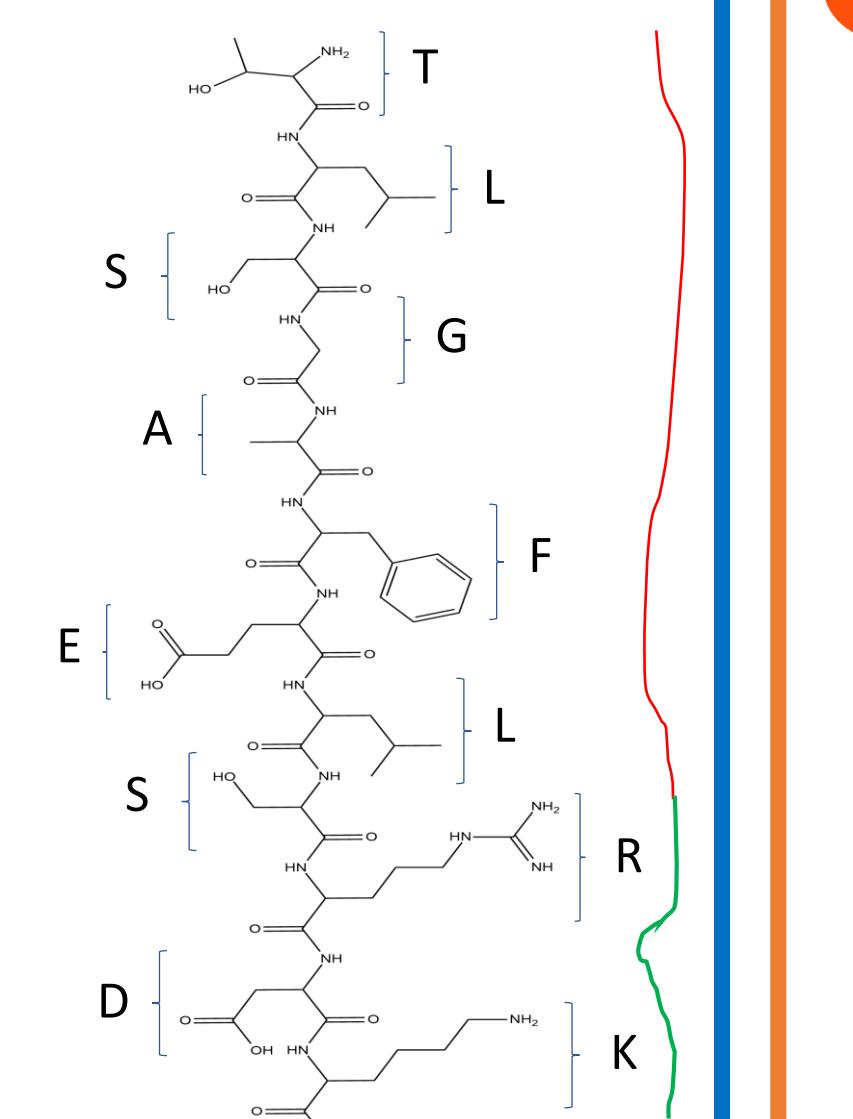
Lipid nanocapsules process



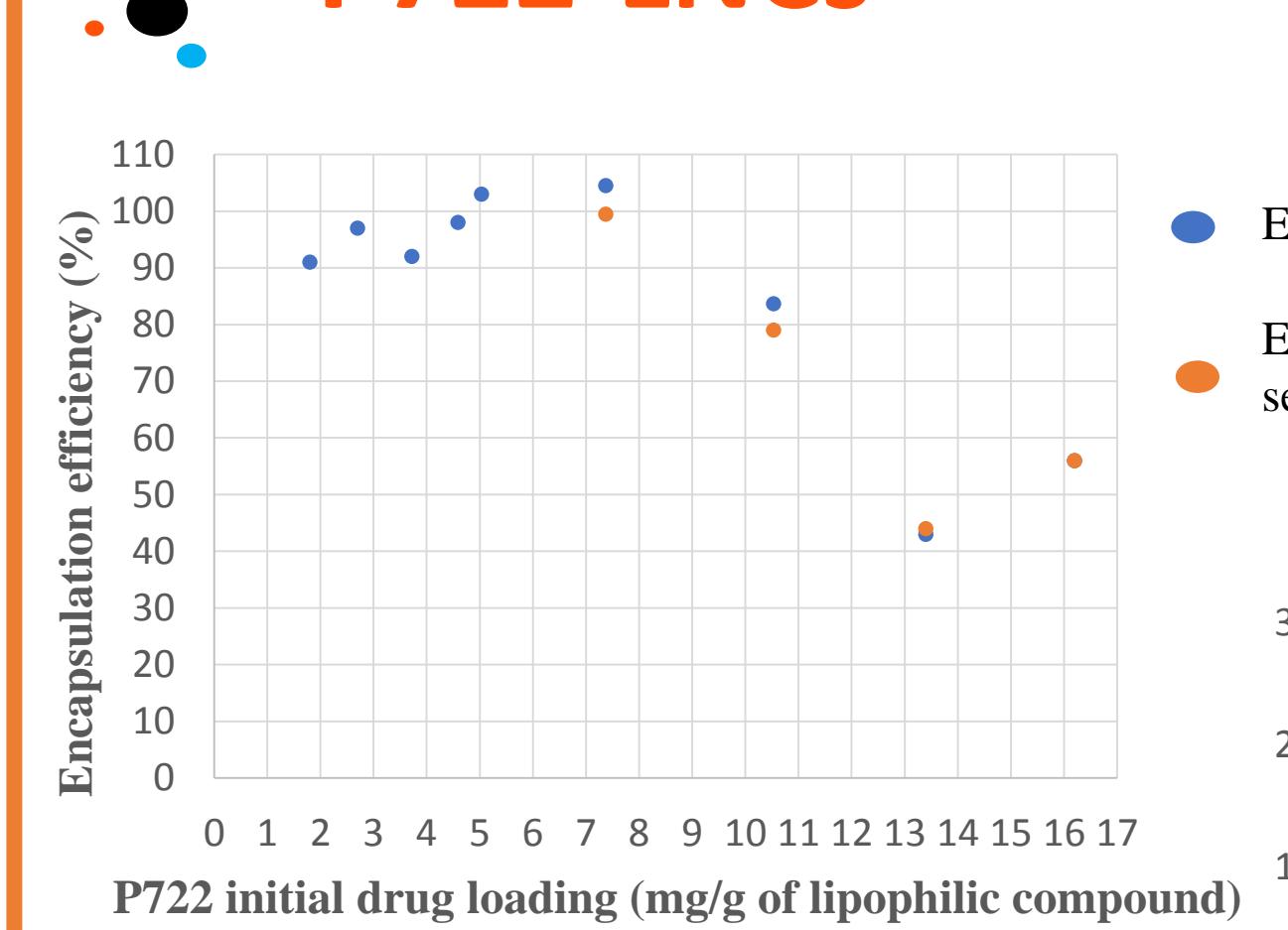
Phase inversion process



TLS peptide
(by Solid phase synthesis)

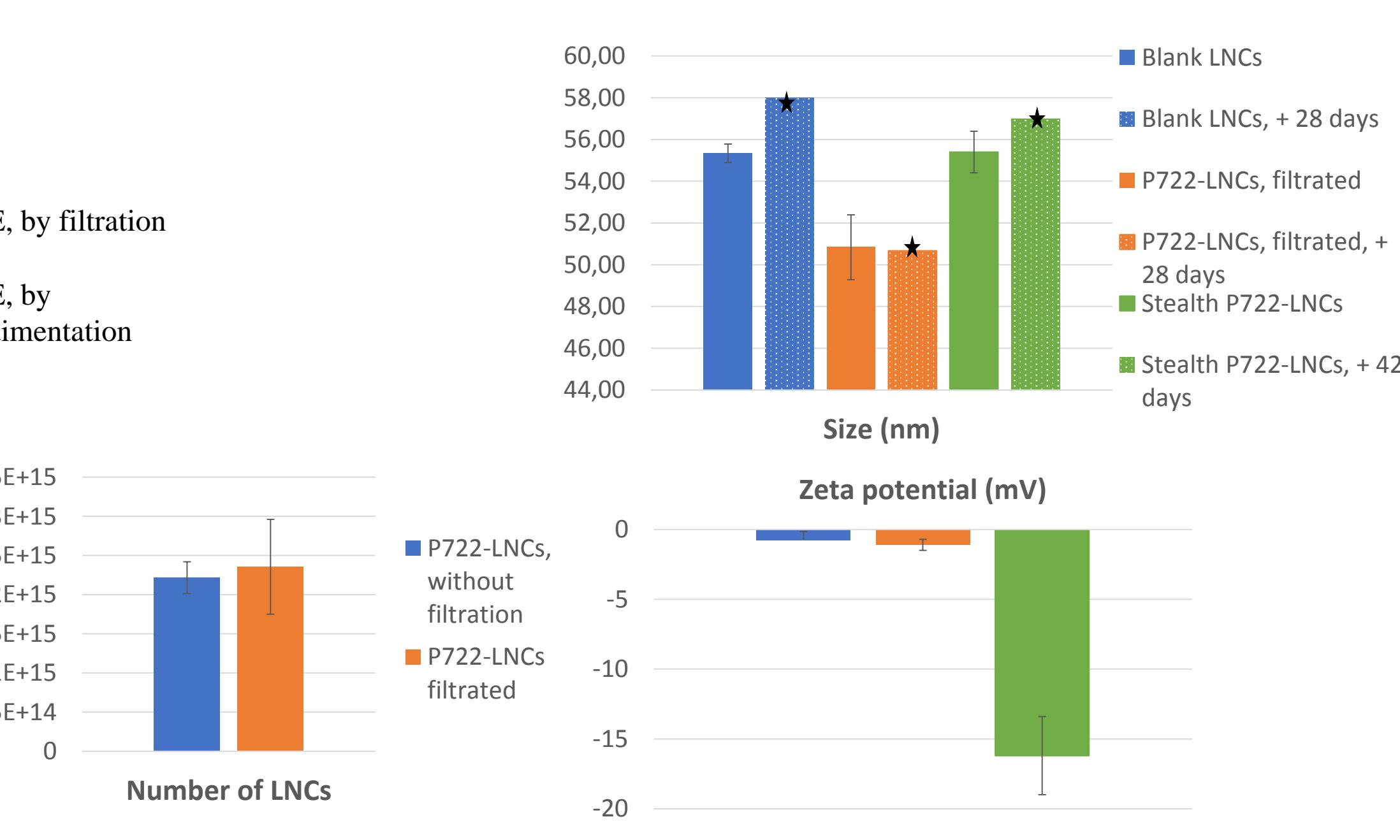


P722-LNCs

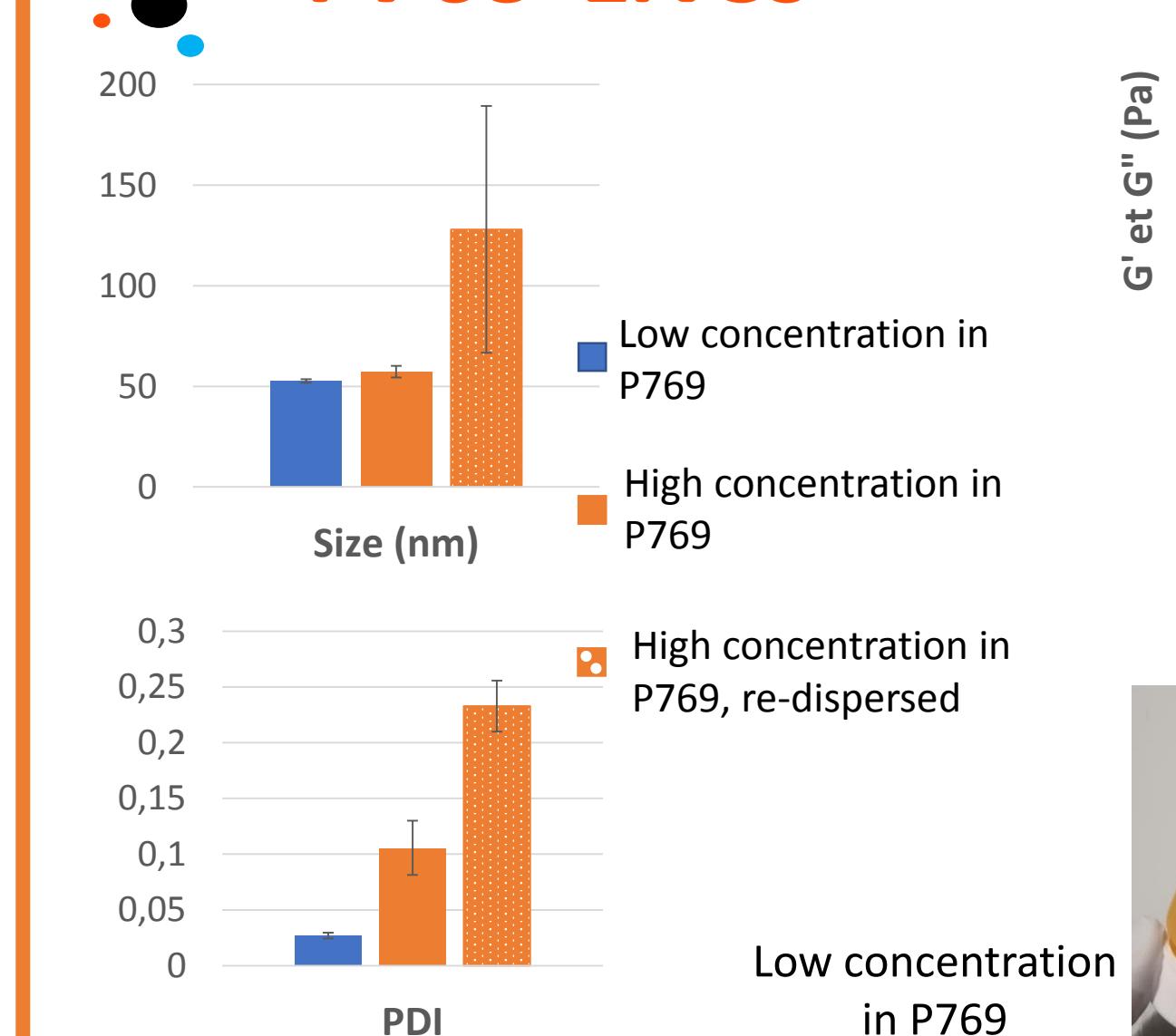


Drug loading max (mg/mL)	Encapsulation efficiency (%)
2	99,5 ± 5,5 (n=4)

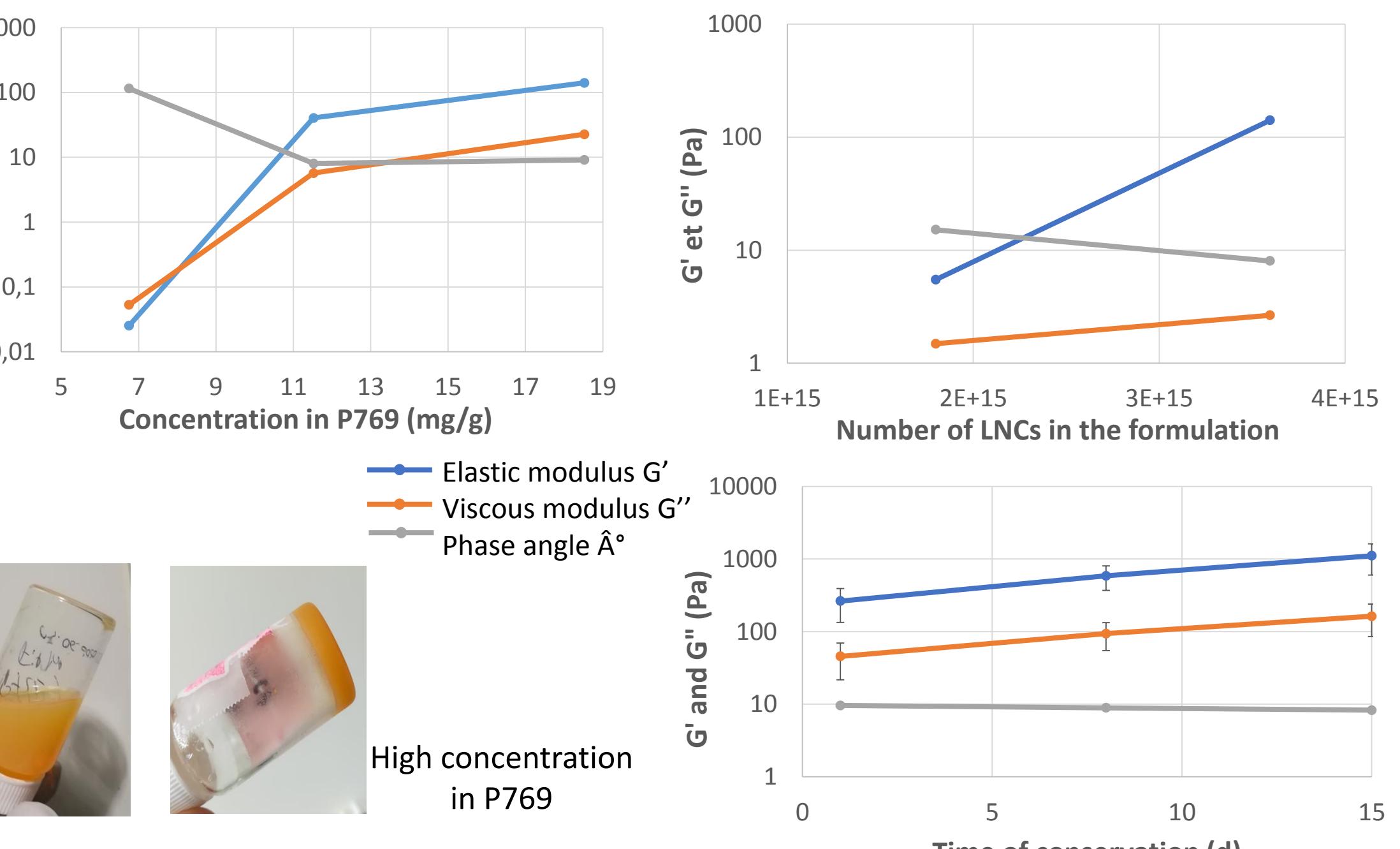
Number of LNCs



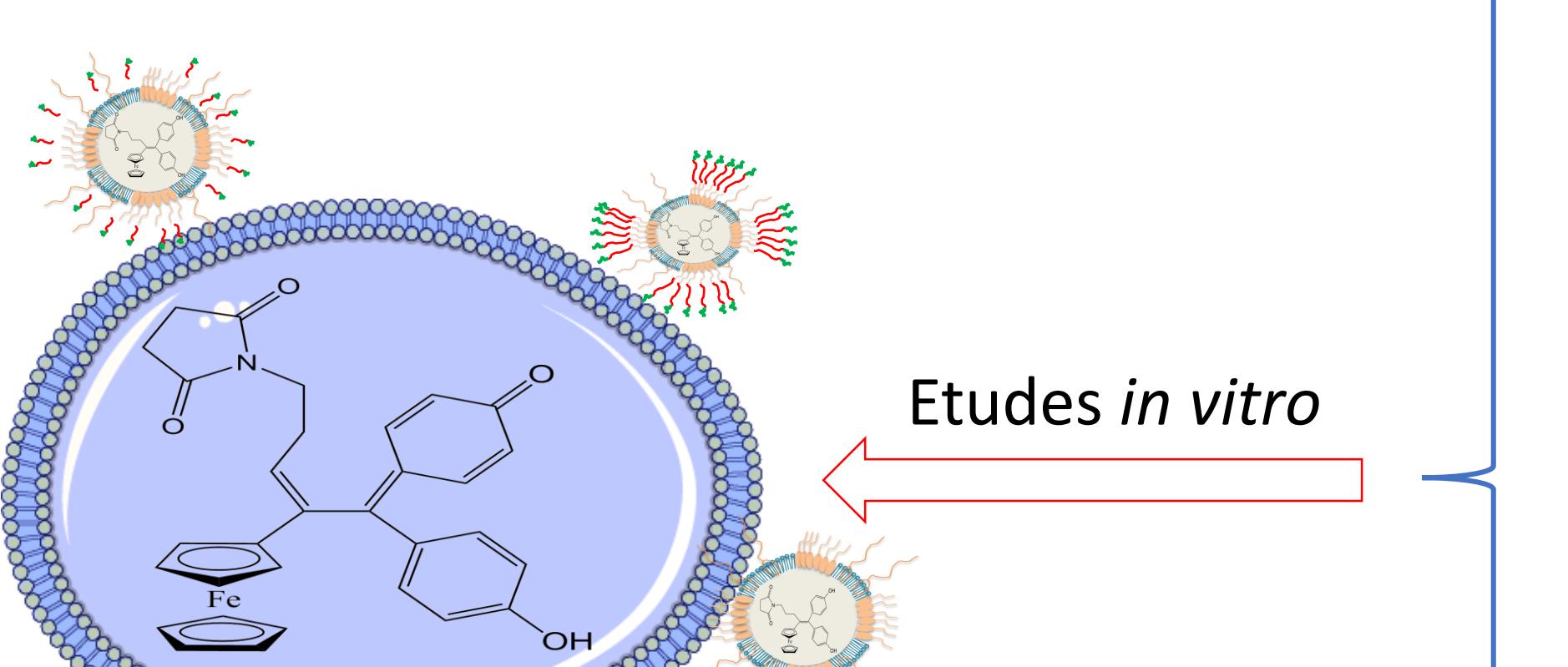
P769-LNCs



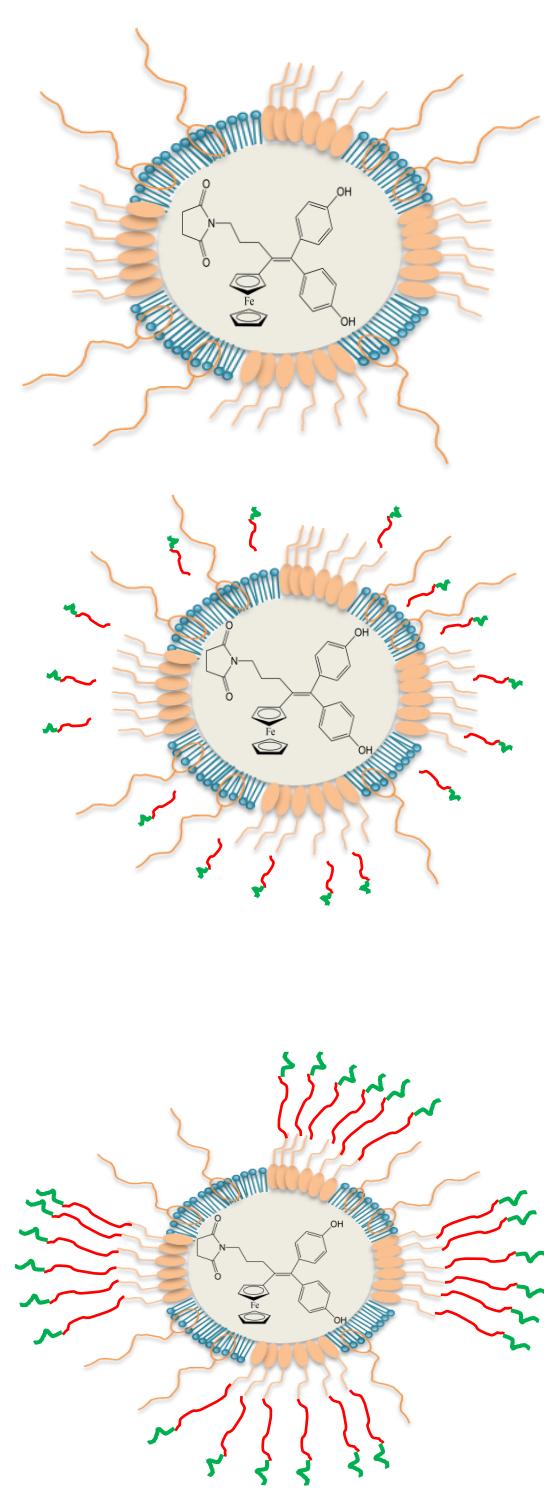
Low concentration in P769



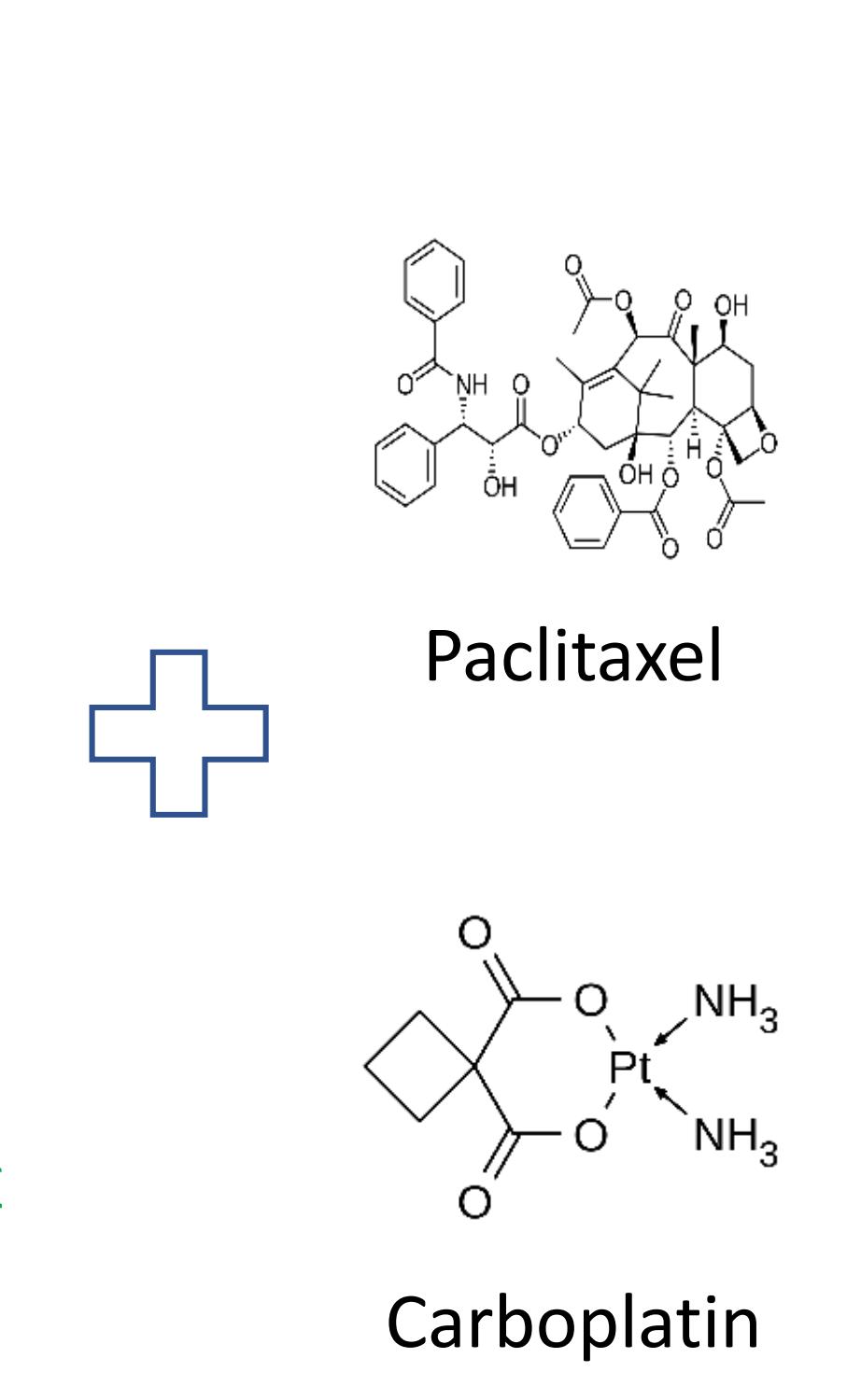
In vitro and in vivo experiments



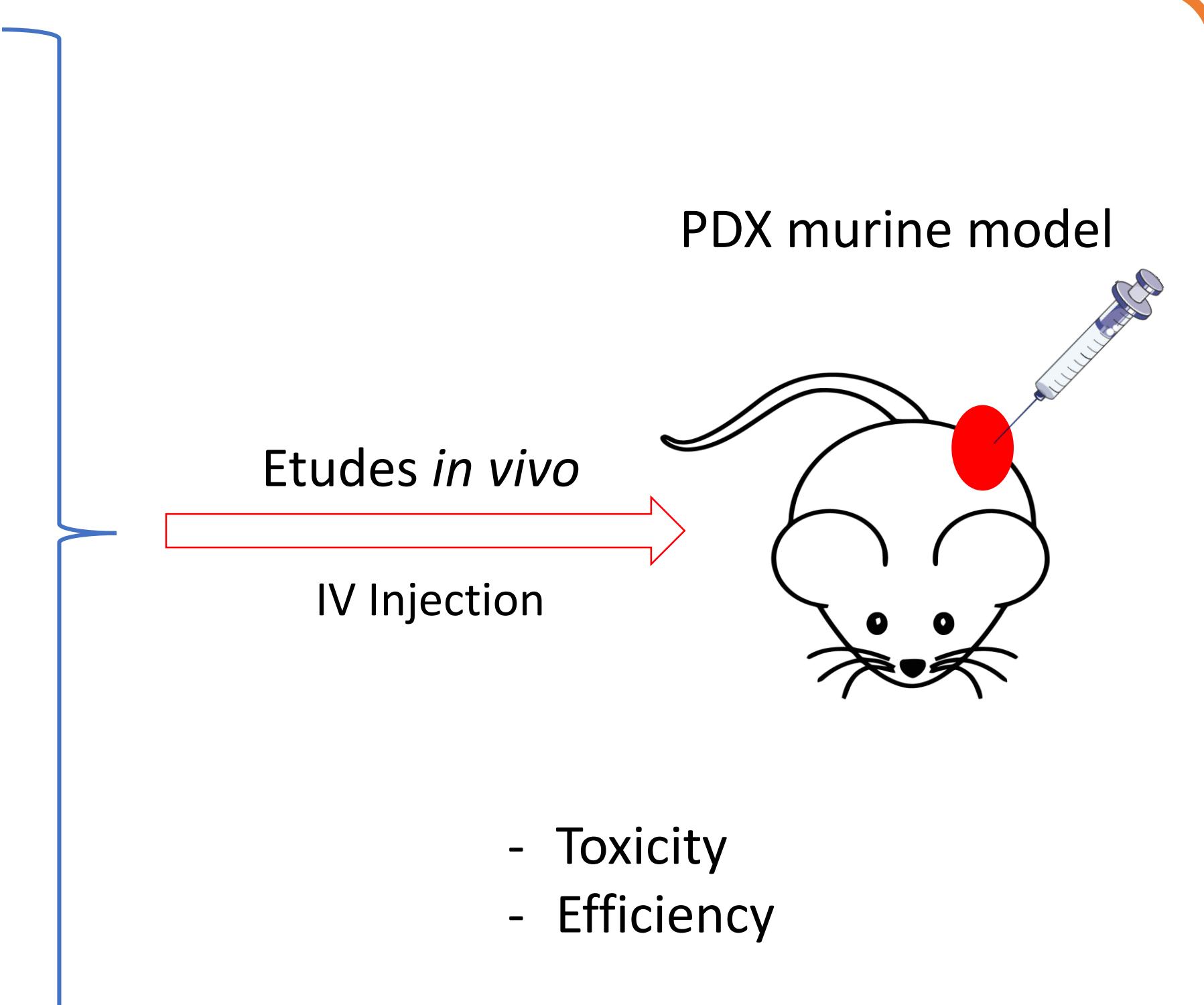
SKOV3 cells



- Cells viability
- Cells internalization
- Cells cycle



- Paclitaxel



- Toxicity
- Efficiency

Conclusion

Different formulations of ferrocifen-loaded LNCs have been obtained. For the physico-chemical characteristics, the results have shown no significant variation of the nanosystems over a period of one month. Interestingly, the encapsulation of P769 has resulted in the formulation of a gel which seemed dependent on P769 concentration, the number of LNCs and the time of conservation. In the future, in vitro and in vivo experiments will be undertaken to determine the efficiency of these innovative treatments.

References

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