The 7th International Electronic Conference on Medicinal Chemistry (ECMC 2021)
01–30 NOVEMBER 2021 | ONLINE

Melatonin loaded lipid nanoparticles for the treatment of glaucoma

L. Bonilla[1,2] *, G. Esteruelas[1,2], M.L. García[1,2], M. Espina[1,2], E. Sánchez[1,2]

[1] Department of Pharmacy, Pharmaceutical Technology and Physical Chemistry, Faculty of Pharmacy and Food Sciences, University of Barcelona, Barcelona 08028, Spain
[2] Institute of Nanoscience and Nanotechnology (IN2UB), University of Barcelona, Barcelona 08028, Spain

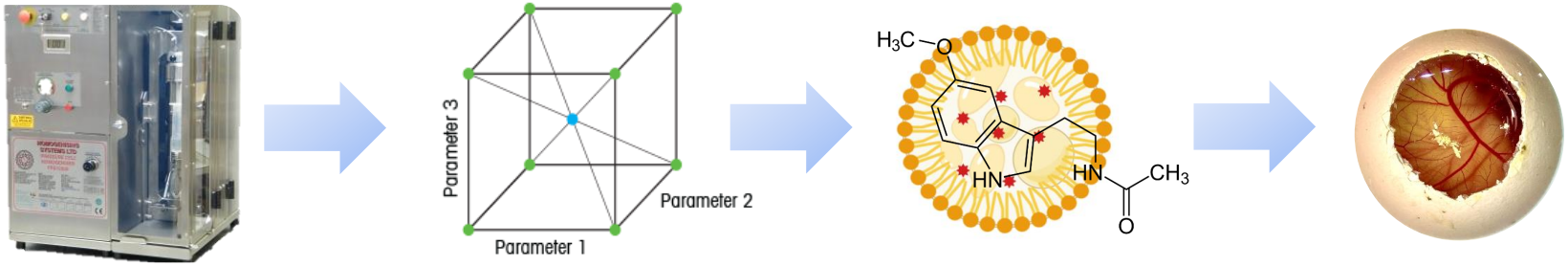
* Corresponding author: Lbonilla95@ub.edu

UNIVERSITAT DE BARCELONA
Facultat de Farmàcia i Ciències de l'Alimentació

IN2UB INSTITUT DE NANOCIÈNCIA I NANOTECNOLOGIA

Melatonin loaded lipid nanoparticles for the treatment of glaucoma

Graphical Abstract



Preparation of NLC | DoE | Optimized MEL-NLC | HET-CAM-TBS

Abstract:

Glaucoma is a multifactorial optic neuropathy, and its most important risk factor is the elevated intraocular pressure (IOP). In this sense, melatonin (MEL), is a neurohormone synthesized in ocular tissues, which regulates IOP. Incorporation of MEL into the last generation of lipid nanoparticles (NLC) constitute a suitable strategy to enhance its efficacy in the retinal tissues.

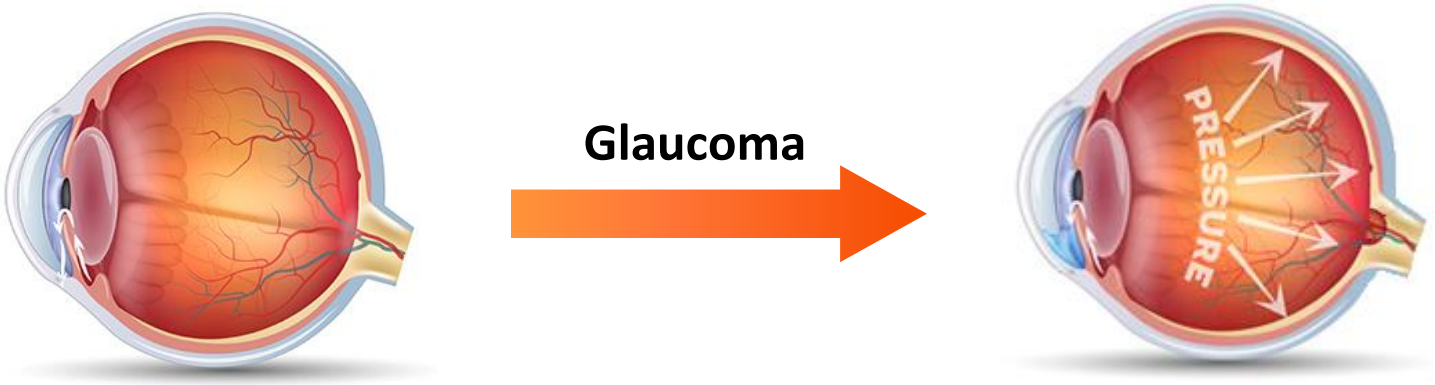
Therefore, the purpose of this work is the encapsulation of MEL into NLC to decrease IOP. MEL-NLC production was carried out by hot high-pressure homogenization and their optimization was performed using the design of experiments approach by examining independent parameters and their influence on MEL-NLC properties (size, polydispersity index, zeta potential and encapsulation efficiency). *In vitro* ocular tolerance was studied using embryonated eggs by means of a quantitative-modified HET-CAM test using trypan blue staining (HET-CAM-TBS) to measure membrane damage.

The optimized formulation had a mean average size below 150 nm, a polydispersity index lower than 0.3, a zeta potential around 20 mV and an encapsulation efficiency above 50%. The *in vitro* ocular tolerance of MEL and MEL-NLC was studied by HET-CAM-TBS test. The results revealed an optimal ocular tolerance for both MEL-NLC and MEL solution, which can be classified, according to the trypan blue adsorption, as a non-irritant.

In conclusion, a novel formulation of MEL-NLC has been developed and optimized with suitable physicochemical parameters for glaucoma treatment showing an optimal ocular tolerance.

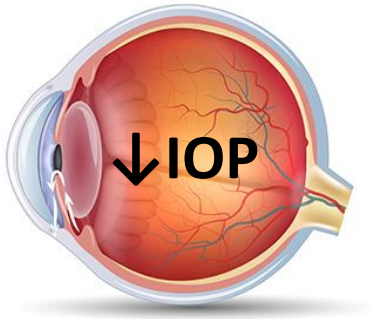
Keywords: lipid nanoparticles; glaucoma; drug delivery

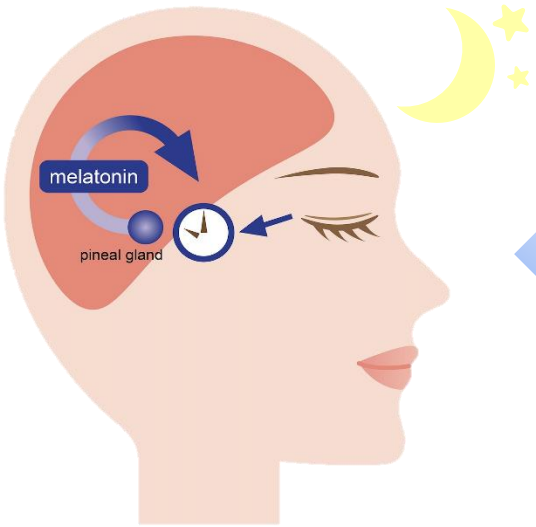
Introduction

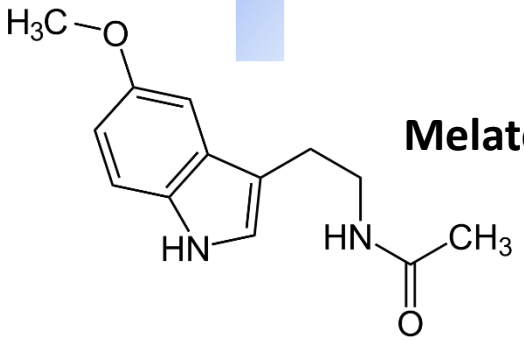


- One of the leading causes of blindness worldwide
- Multifactorial disease
- Elevated intraocular pressure (IOP)
- Non-effective treatment available

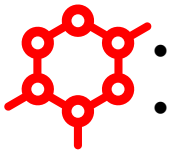
Introduction





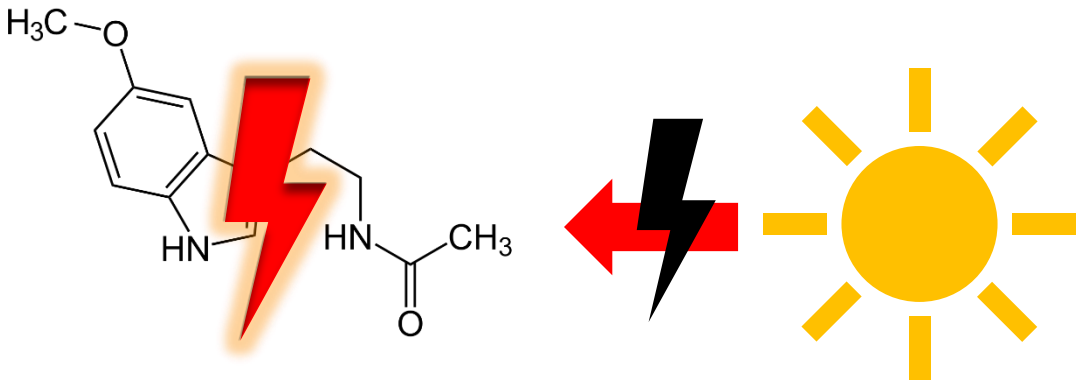


Melatonin (MEL)

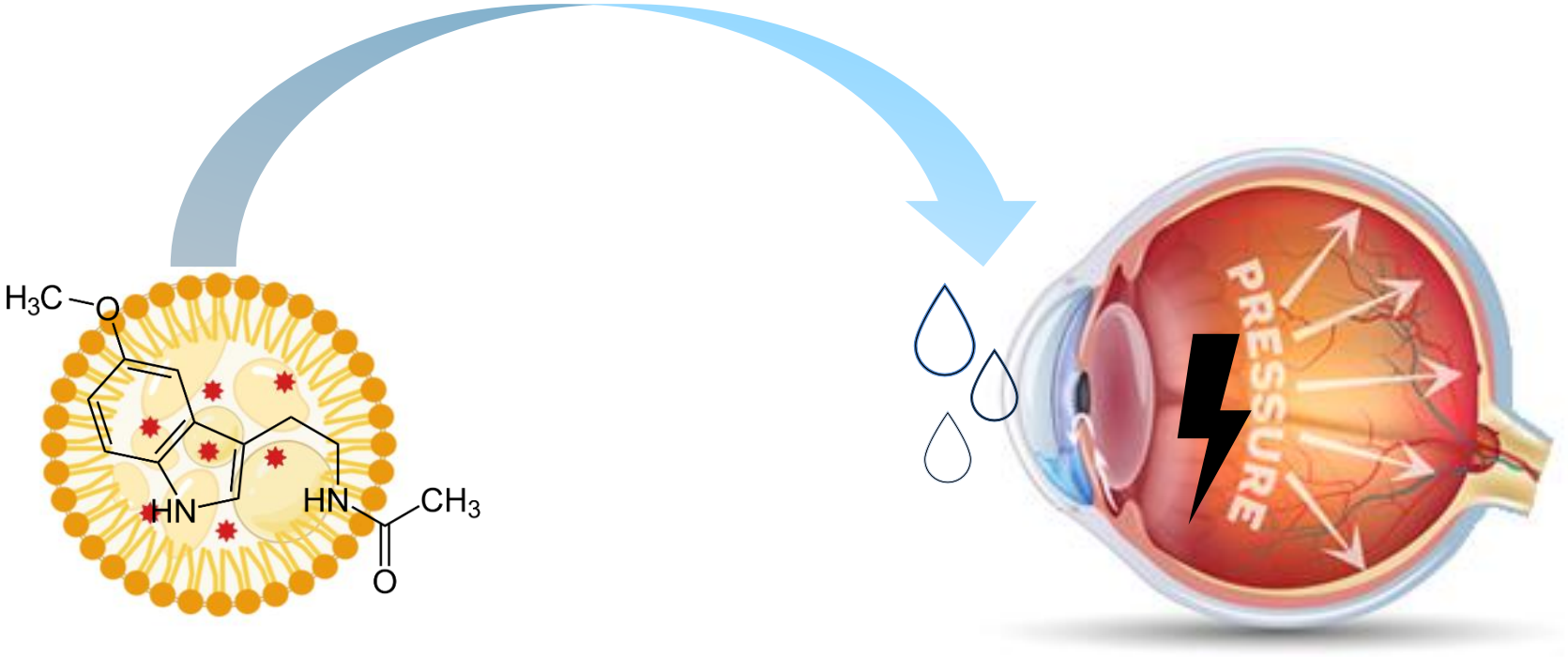


- Anti-inflammatory
- Antioxidant

Introduction



Introduction



Results and discussion

Preparation method

Hot high-pressure homogenization

DoE

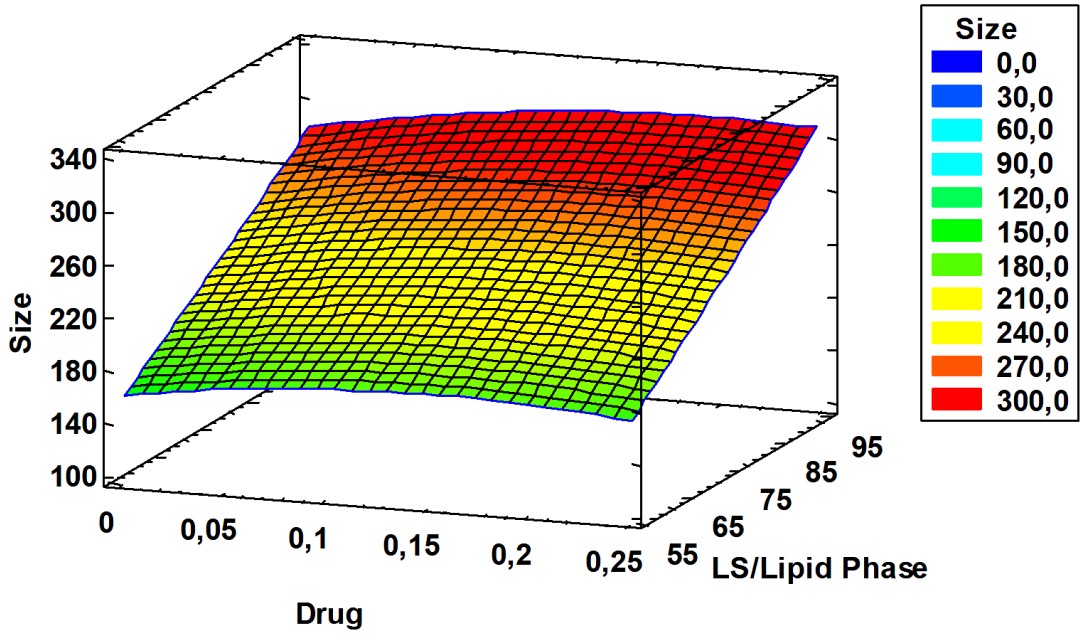
Independent parameters

- Size (nm)
- PDI
- ZP (mV)

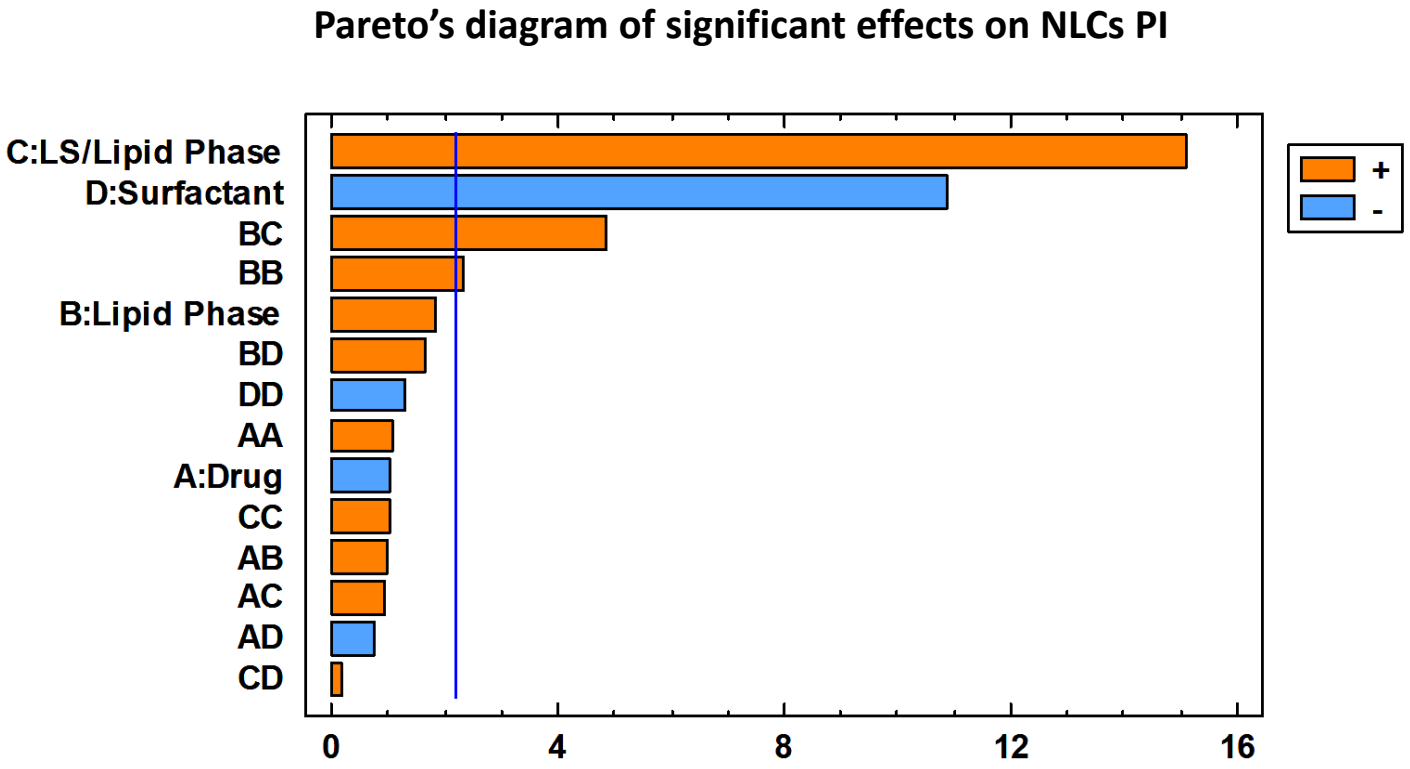
- EE (%)

Results and discussion

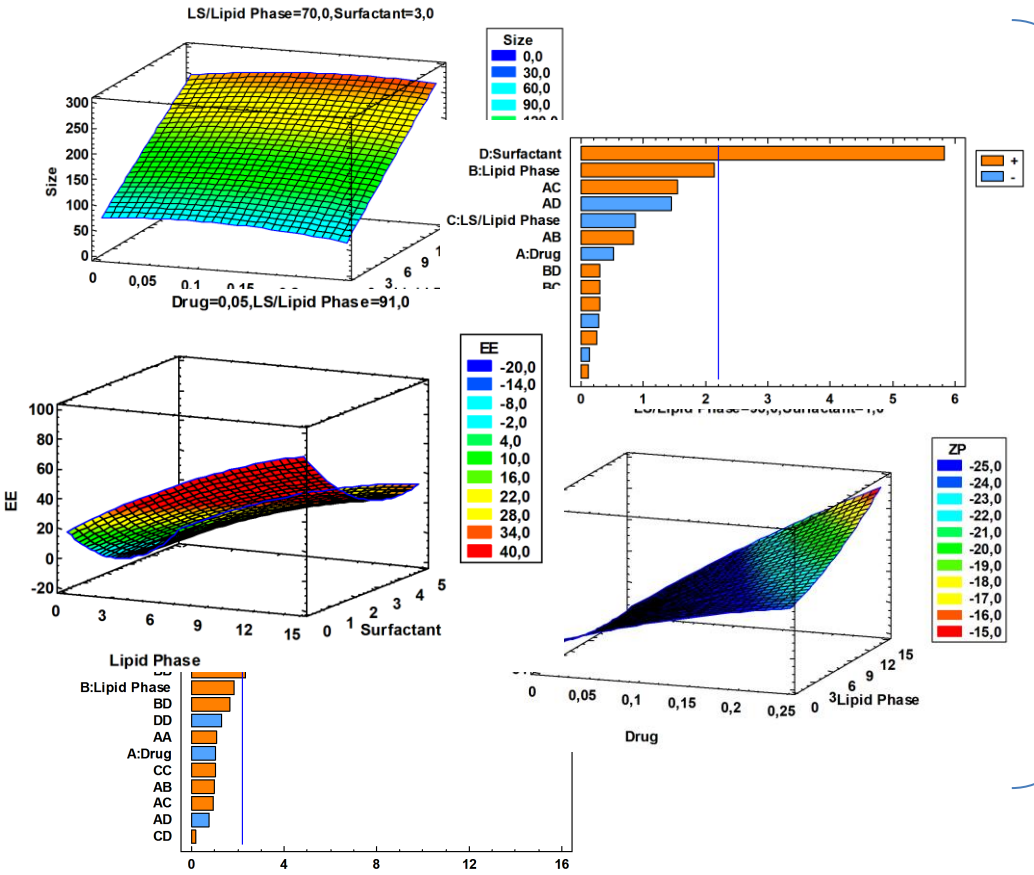
Surface response plot of the effect of the lipid solid and drug on the average size.



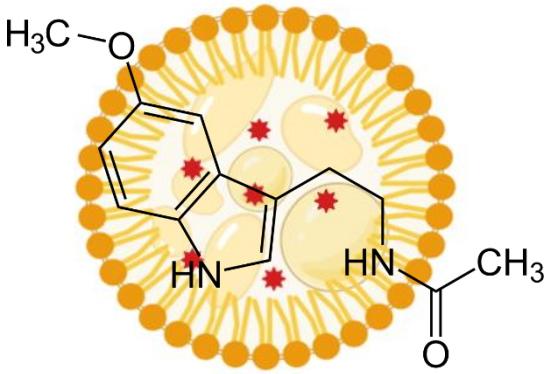
Results and discussion



Results and discussion



Optimizated formulation



Size ≈ 150 nm

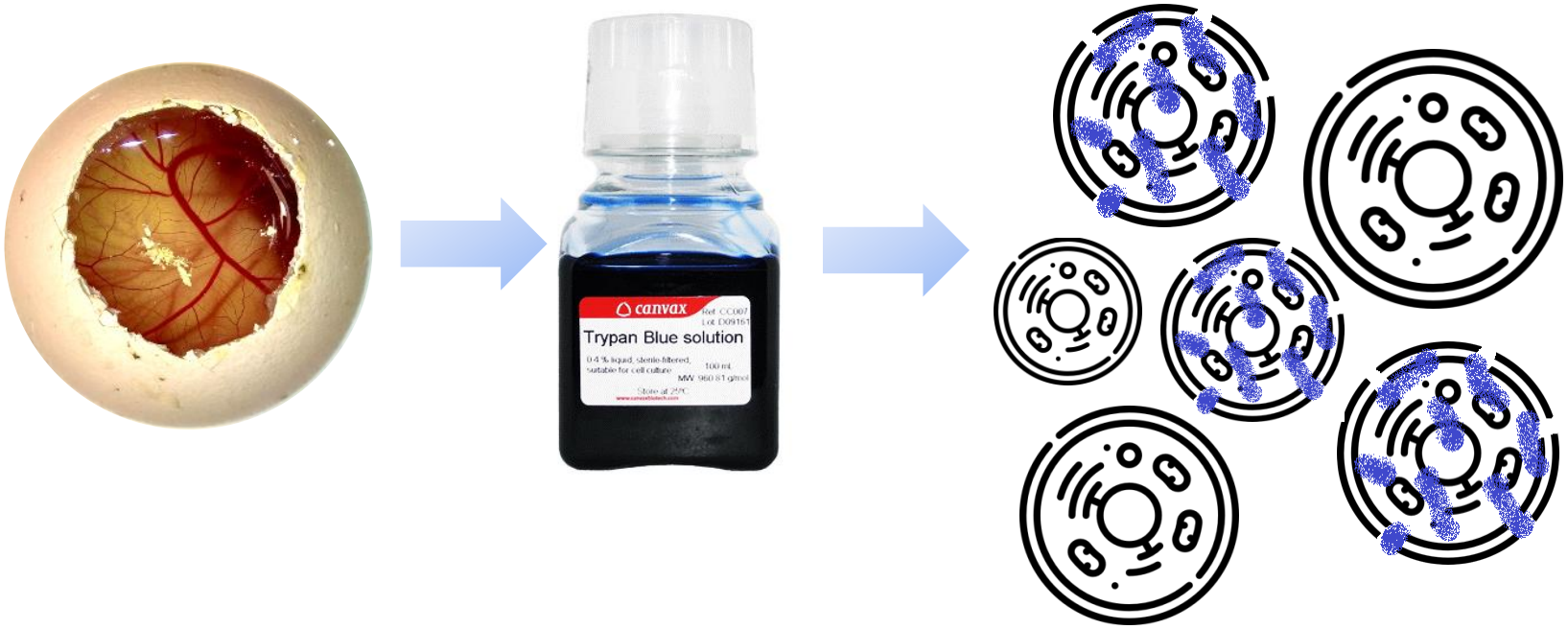
PDI < 0.3

ZP ≈ 20 mV

EE ≈ 50 %

Results and discussion

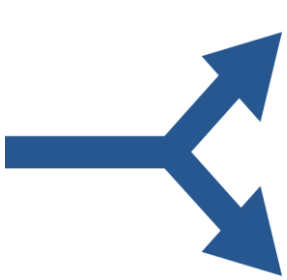
In vitro ocular tolerance: HET-CAM-TBS



Results and discussion

***In vitro* ocular tolerance: HET-CAM-TBS**

QA (nmol/mg)	Classification
≤ 0.10	Non-irritant
0.10 – 0.15	Moderately irritant
≥ 0.15	Irritant



MEL-NLC → non-irritant

MEL solution → non-irritant

Conclusions

- Encapsulation of MEL into NLC
- Optimized with suitable physicochemical parameters
- Optimal ocular tolerance

Acknowledgments

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i Ciències de l'Alimentació

INSTITUT DE NANOCIÈNCIA
I NANOTECNOLOGIA

Generalitat
de Catalunya

Corresponding author: Lbonilla95@ub.edu