The 8th International Electronic Conference on Medicinal Chemistry (ECMC 2022)

01–30 NOVEMBER 2022 | ONLINE

Optimization by Machine Learning of lipid-based Ceftriaxone delivery system

Chaired by DR. ALFREDO BERZAL-HERRANZ;
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pharmaceuticals MDPI

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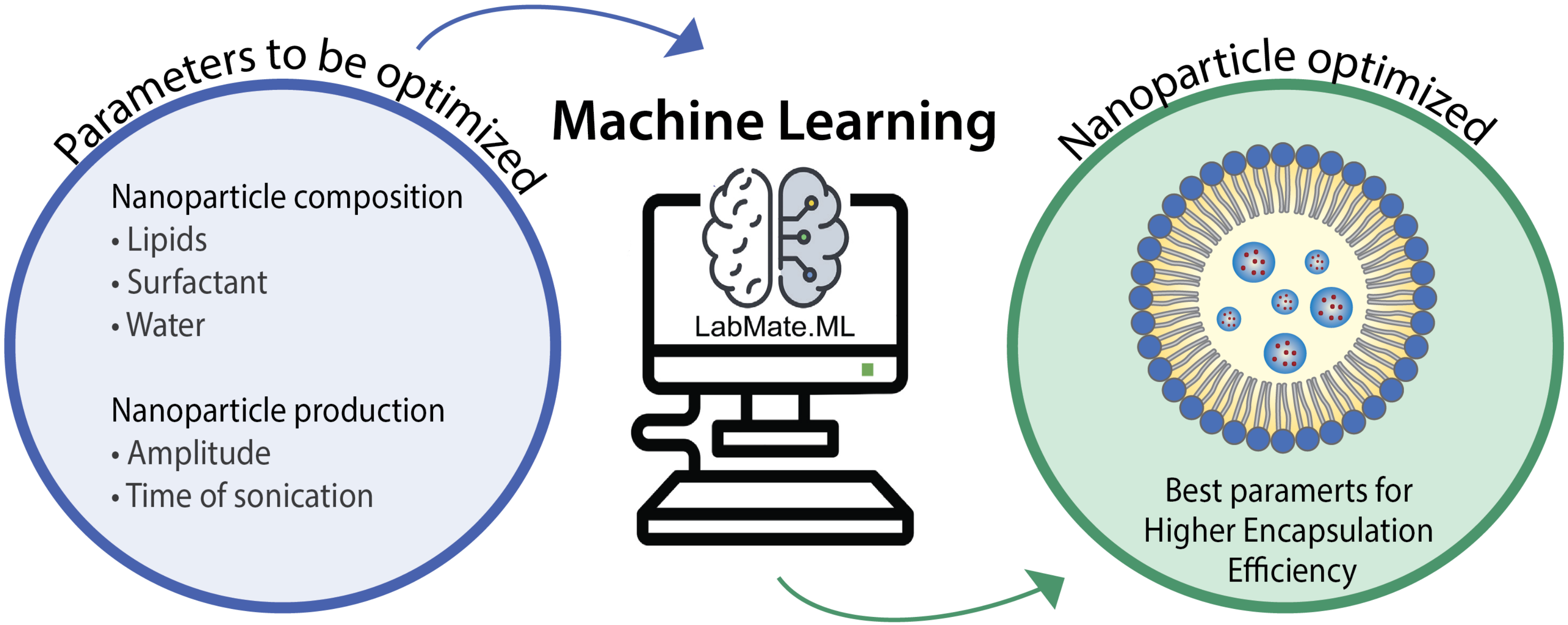
Optimization by Machine Learning of lipid-based Ceftriaxone delivery system



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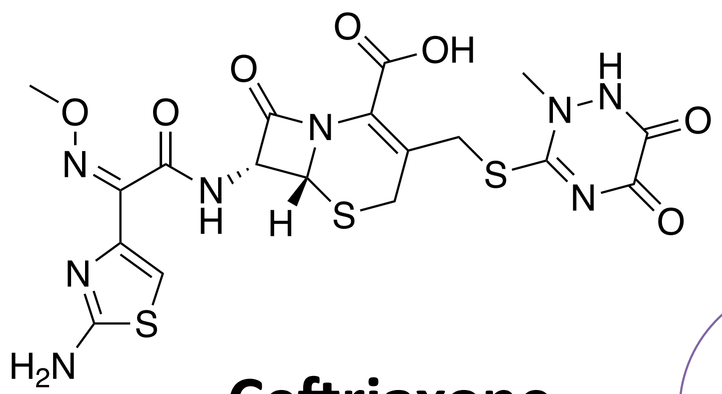
Abstract:

Ceftriaxone (CTX) a third-generation cephalosporin, is a broad-spectrum antibiotic that can be used by intramuscular or intravenous routes to treat various types of infection. However, CTX has poor cellular penetration and poor diffusion due to its high molecular weight and high hydrophilicity. To address these problems, we propose an innovative nanotherapy based on the encapsulation of CTX in a nanostructured lipid carrier. Usually, several attempts must be done, on a trial-and-error basis, until a formulation that guarantees high drug encapsulation and suitable physicochemical properties is found. Machine Learning (ML) has recently stirred great interest as a tool to model and predict the nanoparticles biological activity. Herein, for the first time, the use of ML for the optimization of a nanoformulation is explored. Several variables were optimized simultaneously, namely the amount of solid lipid, the percentage of liquid lipid, the surfactant solution, the water volume, the sonication amplitude, and the sonication time. To define the best nanoformulation, three different outcomes were considered: encapsulation efficiency of CTX, size of the nanoparticles and their zeta potential. Our ML approach was able to find, with a low number of experiments, the conditions that provided formulations with the highest encapsulation efficiency of CTX and nanoparticles with suitable size and adequate zeta potential. Besides the impressive acceleration of the optimization process that was achieved, the optimization guided by our ML model also provided insights over the optimization of other nanoformulations.

Keywords: Ceftriaxone; Lipid-based nanocarriers; Machine Learning; Optimization

Ceftriaxone (CTX)

Why this drug?



Ceftriaxone

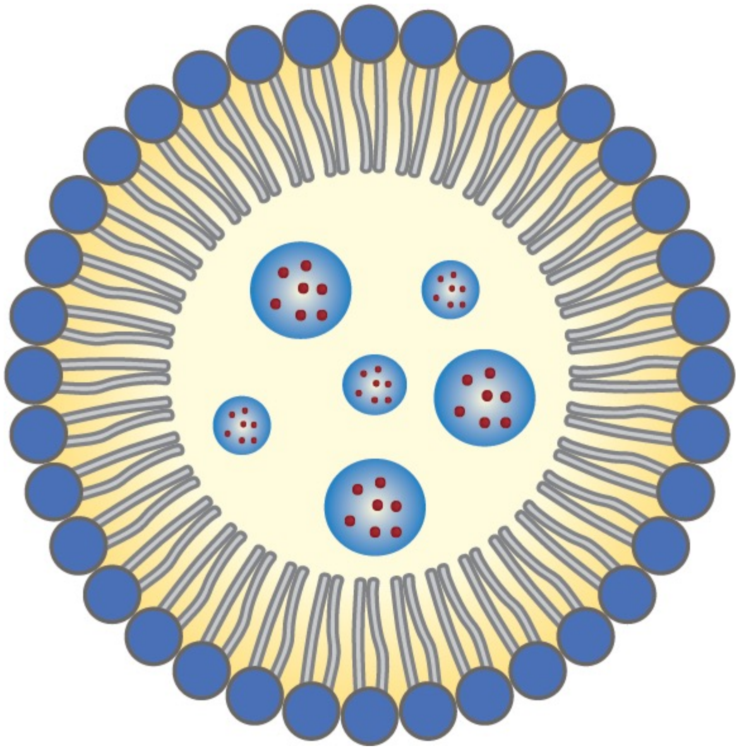
Ceftriaxone (CTX) is a third-Generation Cephalosporin with activity against to *Staphylococcus aureus.*

Guidelines: first-line of treatment to various types of infection.

Problems of poor cellular penetration: high molecular weight (661 g mol^{-1}) and the high hydrophilicity (log P -0.6).

Chem. Commun. 2020, 56, 13907-13917; AAPS PharmSciTech 2012, 13, 411-421.

Nanostructured lipid carrier (NLC)



Encapsulation of hydrophilic drugs and precise control of their release are challenging because of their high water-solubility.

Water vacuoles ideal for hydrophilic drugs.

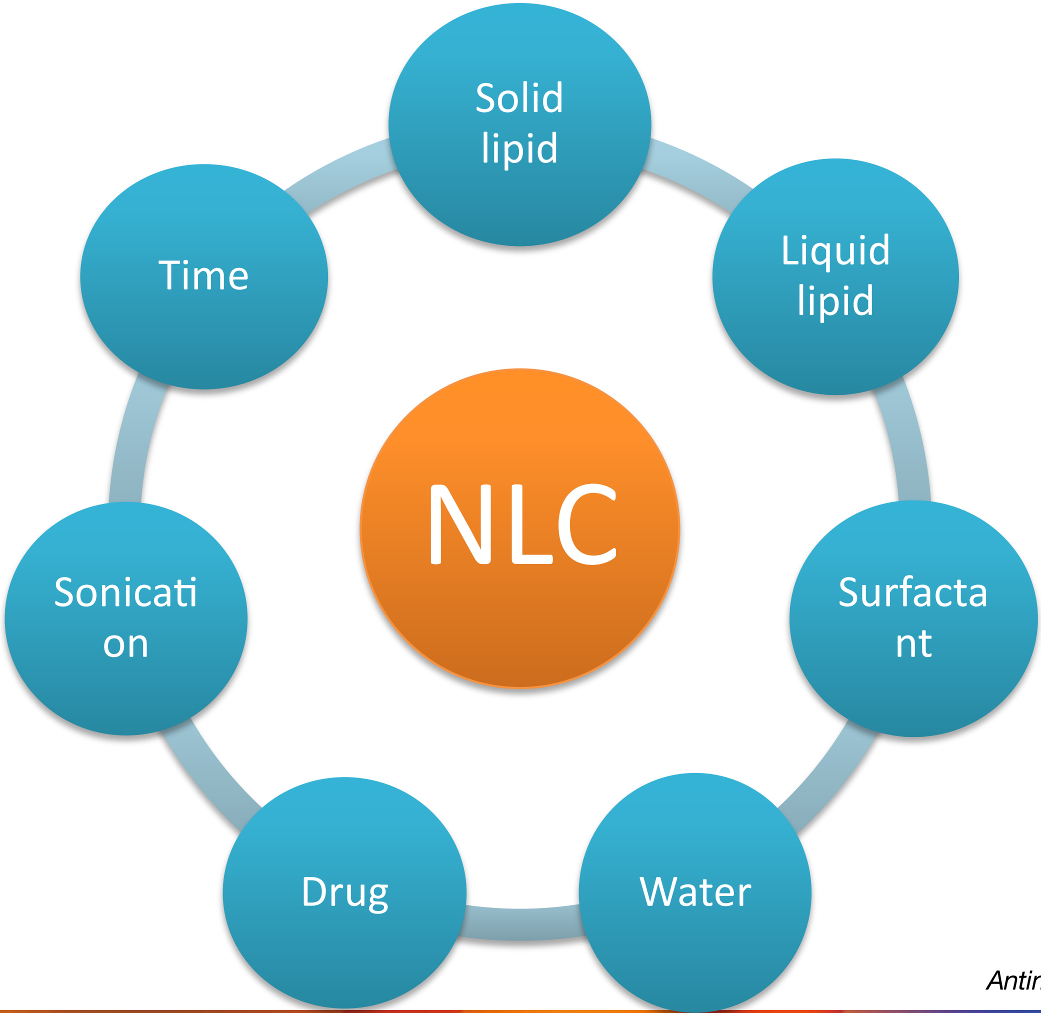
High drug loading capacity.

Long-term stability of incorporated drug during storage.

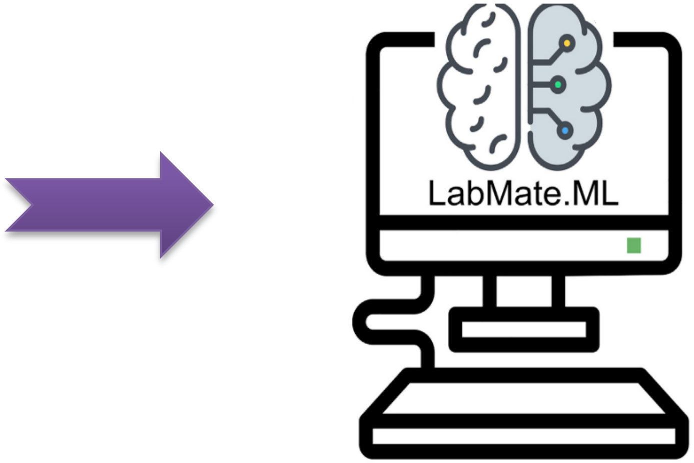
Nanotechnology Reviews, vol. 11, no. 1, 2022, pp. 1744-1777. https://doi.org/10.1515/ntrev-2022-0109

NLCs-CTX

Multi-parametric nanoformulation

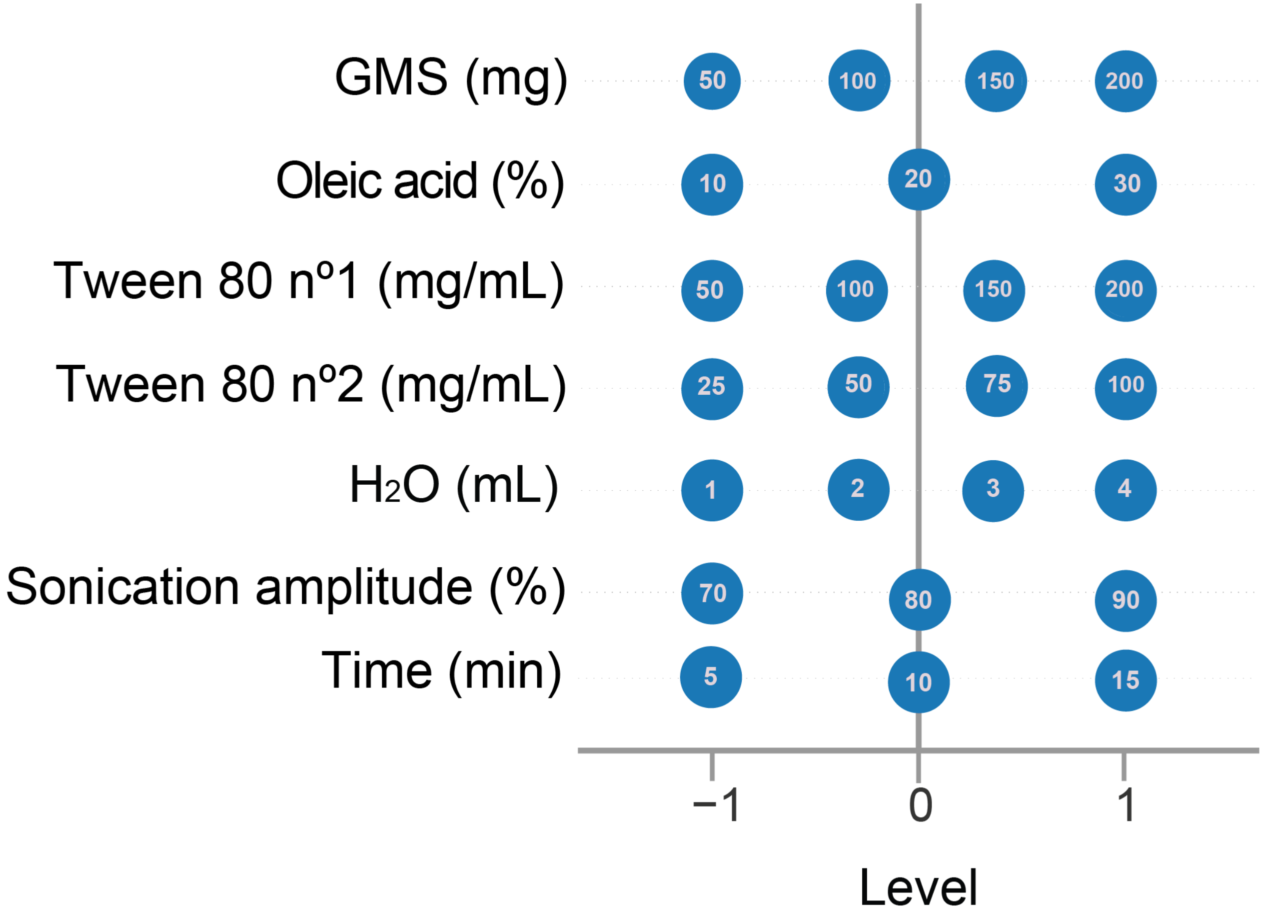


Optimization by Machine Learning



Reker, D. *et al Cell Rep. Phys. Sci.* **2020,** *1* (11), 1-19.
Antimicrob Resist Infect Control **2020**, *9* (1), 28. DOI: 10.1186/s13756-020-0690-4

Reaction Parameters



Outcomes

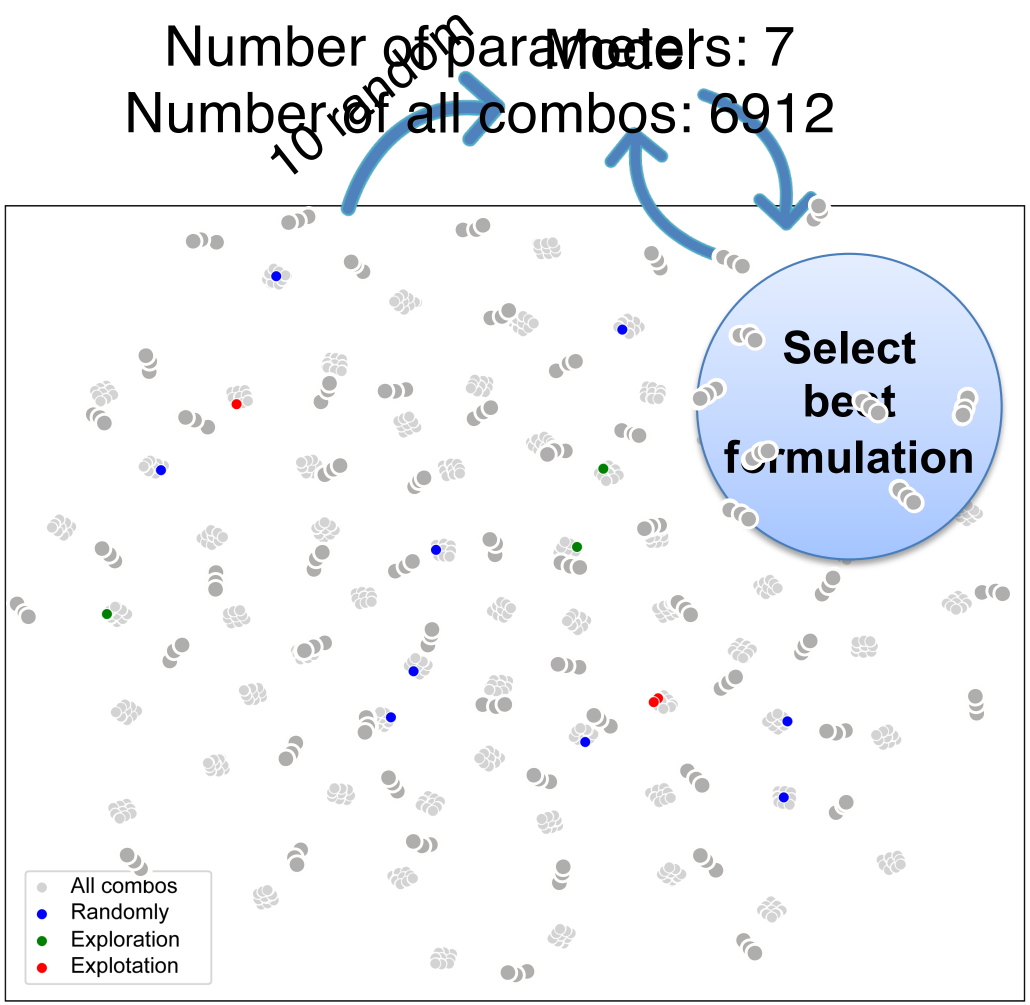
Maximize

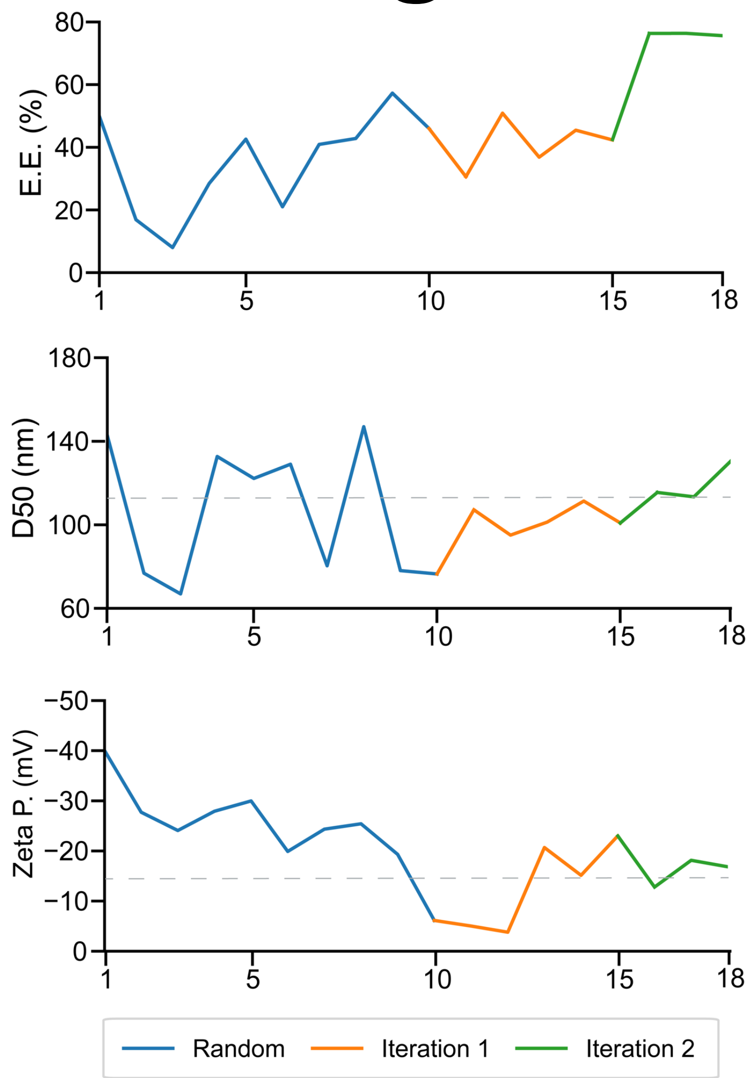
- Encapsulation Efficiency (%EE)

Monotoring:

- Size (D_{50}): >130 nm
- Zeta potencial (ZP): > -20 mV

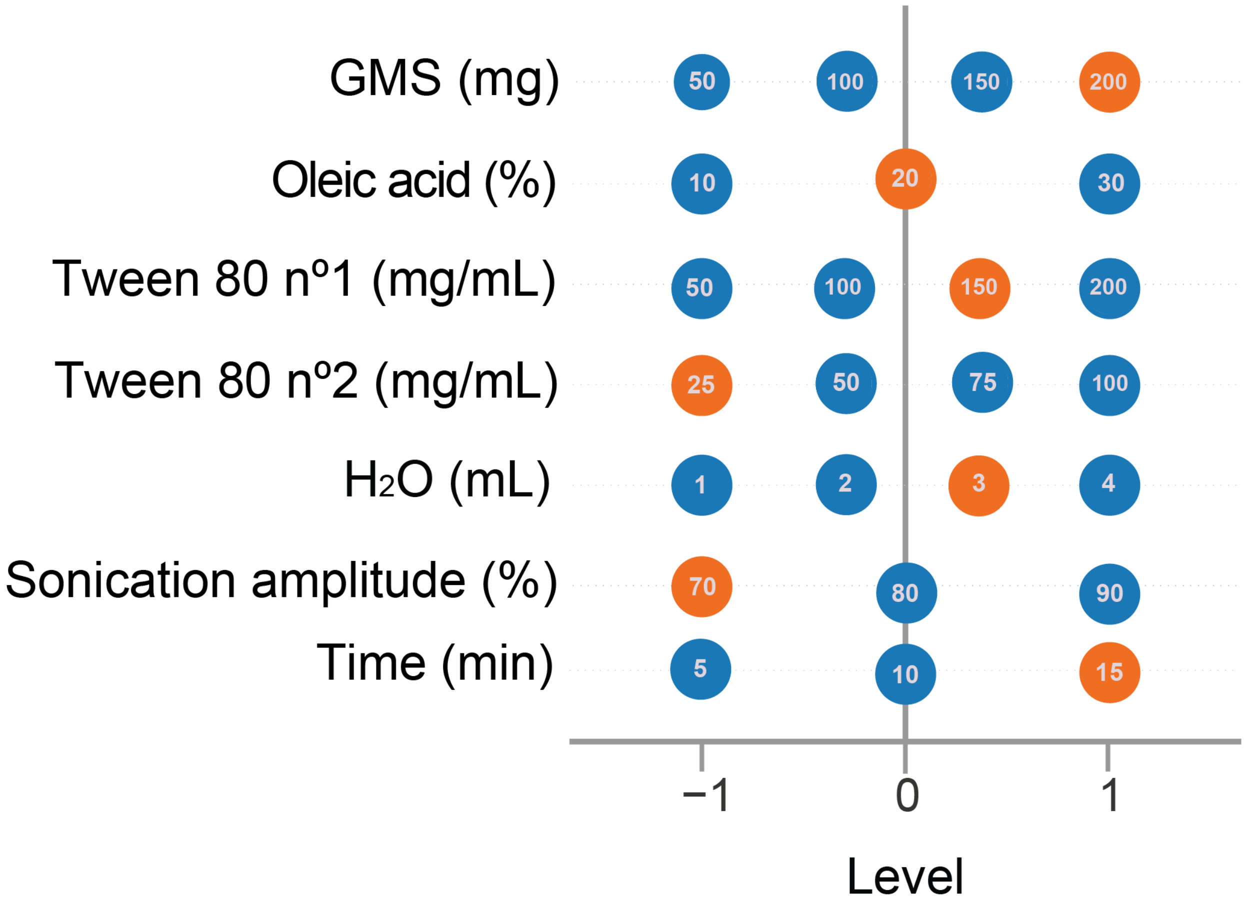
Optimization by Machine Learning





Optimization by Machine Learning

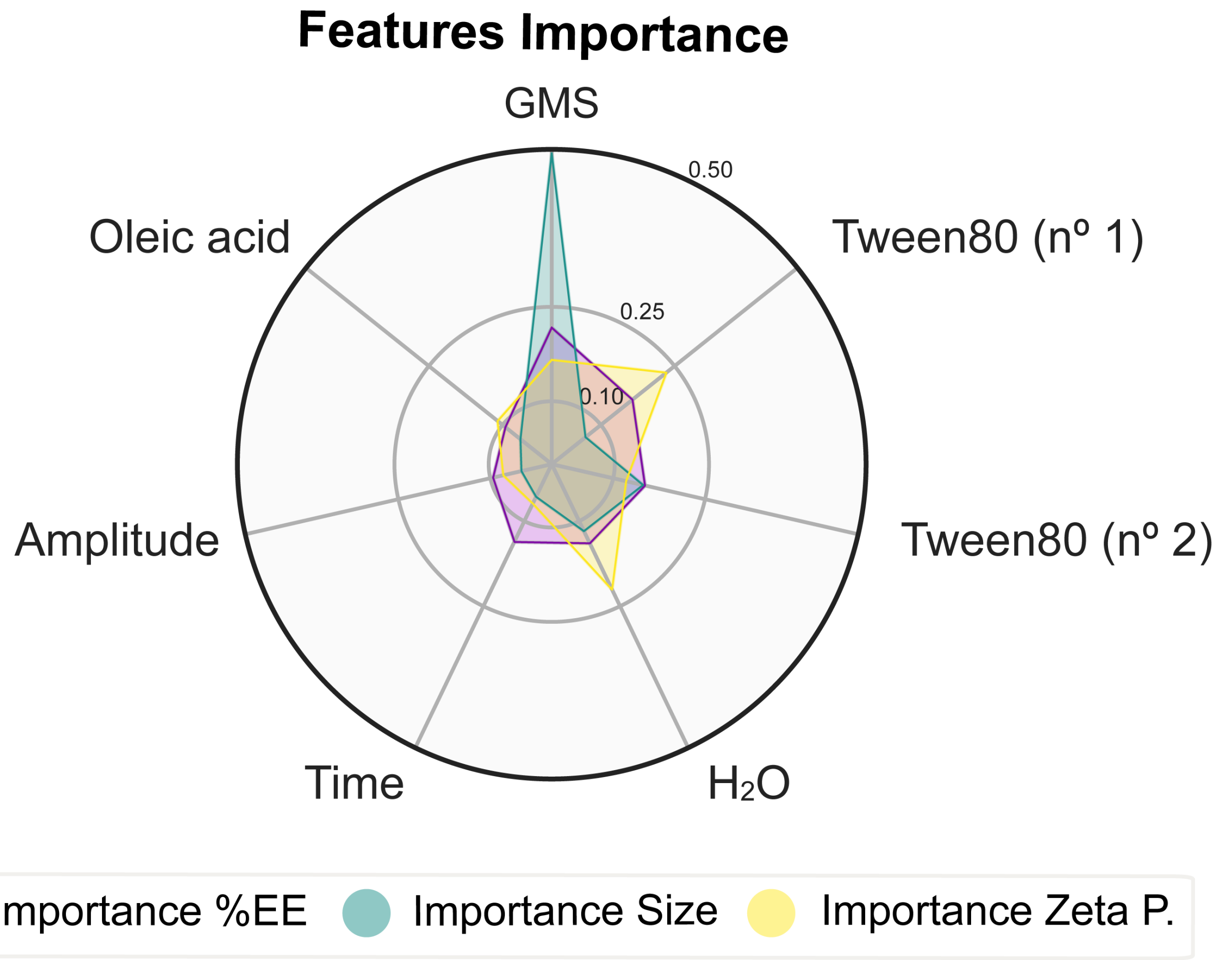
Best parameters



Outcomes:

- Encapsulation Efficiency (% EE): 75.6 %
- Size (D_{50}): 130.4 nm
- Zeta potencial (ZP): -17 mV

Optimization by Machine Learning



Conclusions

6912 formulations

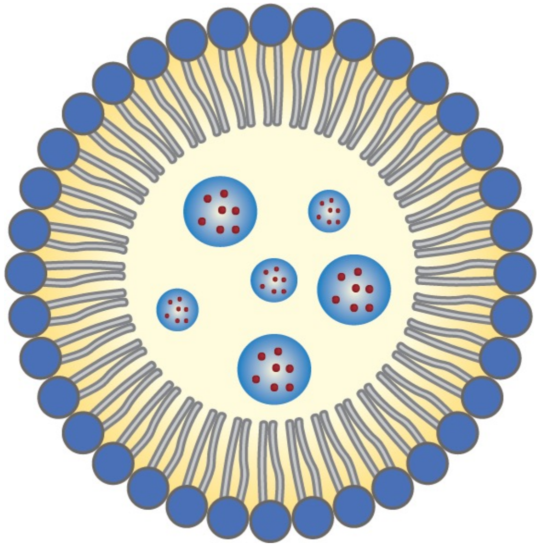
All combinations

18 formulations

Optimization process

1 formulation

Best parameters for one formulation



CTX-NLC

- Higher encapsulation efficiency
- Suitable size and zeta potential

Acknowledgments

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