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PROJECT GOALS

- Production of multifunctional drug delivery system **using biodegradable** and **biocompatible polymers** (PLGA / PLA) to obtain **nanoparticles** (NPs);
- Chemical-physical, morphological and technological-formulation characterization of produced NP;
- Formulation of NPs loaded with **lipophilic drugs** (T3, ibuprofen) through different formulation techniques (nanoprecipitation, surface covalent coating);
- **Prolonged release** over time (min 10 days);

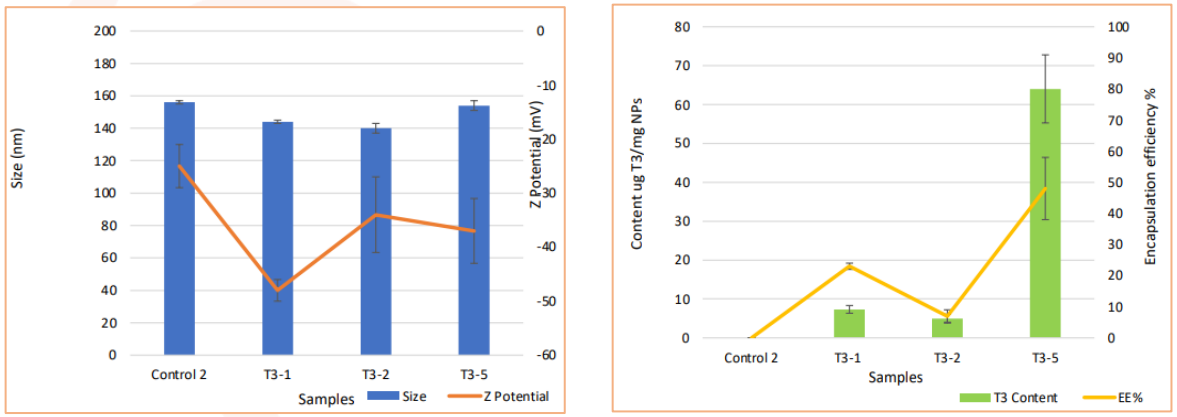
T3 loaded PLGA NPs

T3 NPs formulated by **nanoprecipitation** was optimized varying different parameters (Acetone/DMSO volume ratio: 9:1, 3:1, 1:1; quantity of T3 loaded) to obtain the best formulation in term of chemico-physical and pharmacological characteristics and stability over the time (scheme 1).

Samples	T3 (mg)	Polymer	Organic solution	Water solution
Control-2	0	50mg PLGA	3ml acetone + 1ml DMSO	12,5 ml Pluronic 3% (w/v)
T3-5	5			
T3-2	2			
T3-1	1			

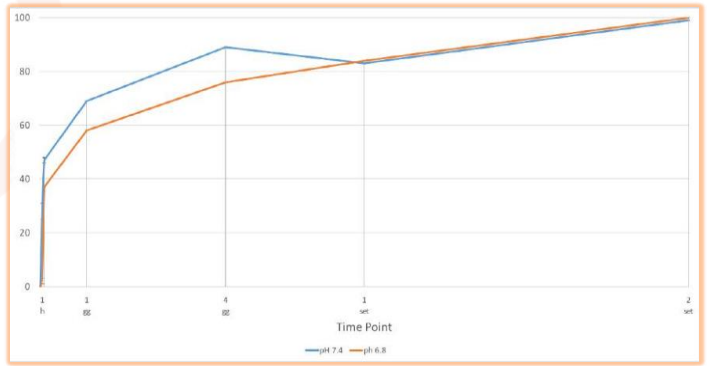
Scheme 1. Formulation parameters of different doses of T3 NPs

NPs based on **PLGA**, loaded with **5 mg T3** and prepared using as organic solution a mixture of Acetone/DMSO (**ratio 3:1**) have proven to be the best formulation.



Scheme 2. Chemico-physical characterization of T3 NPs (left) and pharmaceutical characterization of T3 NPs (right)

Afterwards, the T3 NPs **release** were studied in buffer ACSF pH 7.4 and 6.8 (scheme 3).
The formulation shows an initial **burst release around 50%** of the total drug entrapped.
Then, the **T3 released is modulated over the time until 10 days**.
Currently, ***in vivo*** studies of NPs loaded with T3 are perfomed by project partners.
NPs confirmed dimensional, morphological and stability characteristics previously in optimization content studies.



Scheme 3. Study of T3 NPs in buffer ACSF pH 7.4 and 6.8

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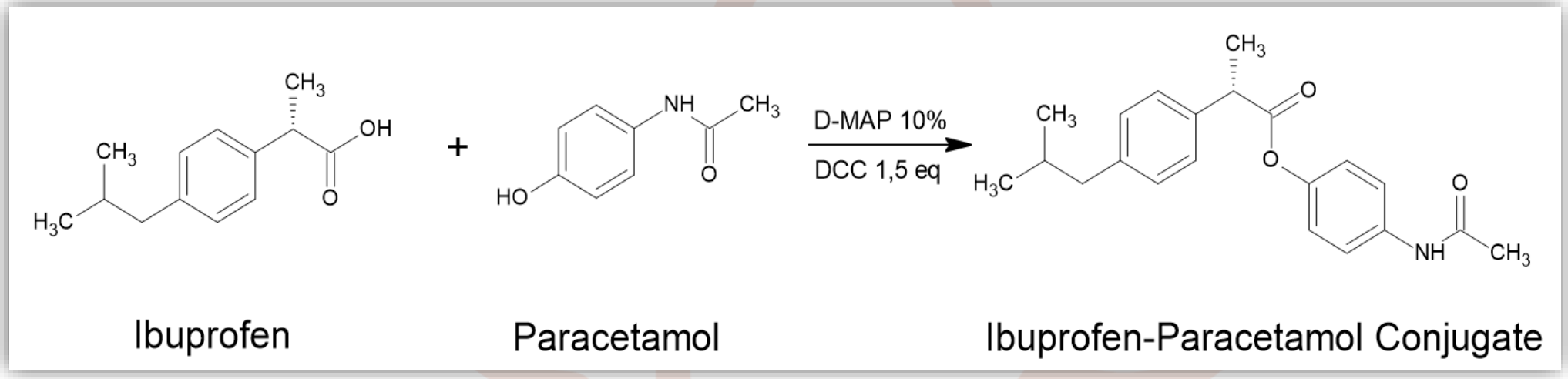
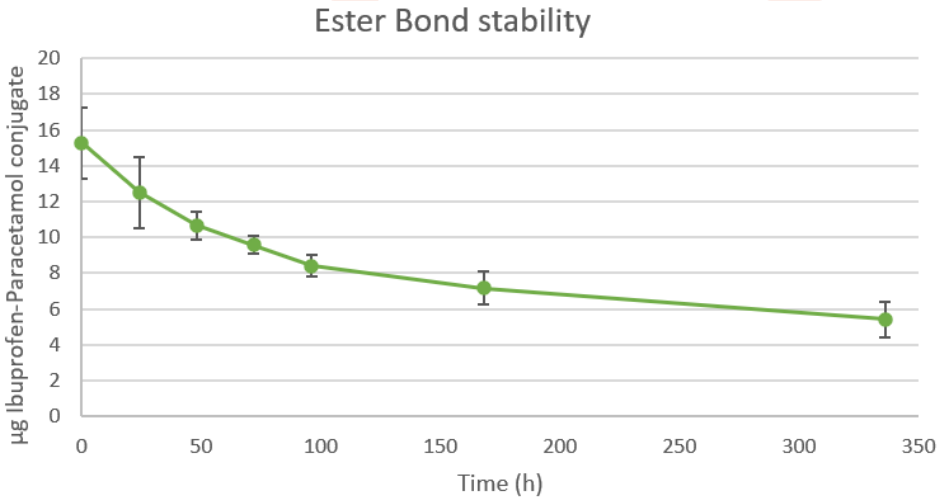
Synthesis Ibuprofen-Paracetamol conjugate (IPc)



•***Ester bond stability studies:***

2ug/ml IPc in buffer at different time point

- Magnetic stirrer
- Temperature: 37°C
- Different time point



Scheme 4. Stability study of the ester bond

- ***Molecular Formula***: $C_{21}H_{25}NO_3$
- ***Molecular Weight:*** 339.4281
- ***Log P***= 4.69

Solubility:

Water	5ug/1ml
Etylacetate	1mg/1,4ml
Acetonitrile	1 mg/ml
Acetone	1 mg/ml
Dimethyl sulfoxide	1mg/620ul
chloroform	1mg/563ul
Dichloromethane	1mg/500ul
Methanol	1mg/153ul

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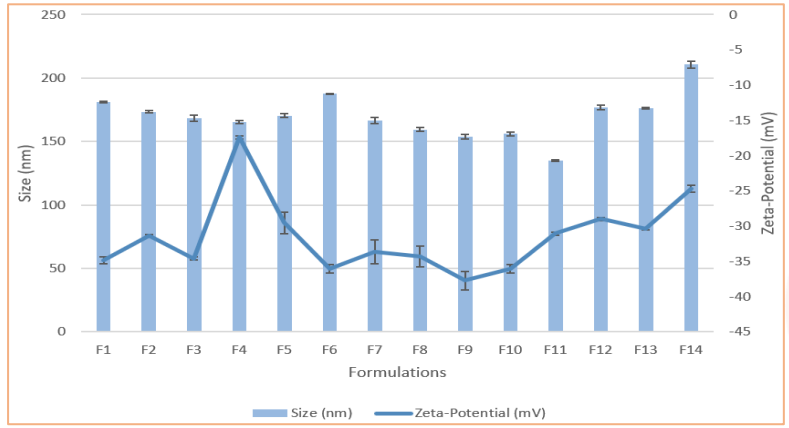
Characterization of Ibuprofen-Paracetamol NPs formulations

5mg of IPc loaded into **polymeric NPs** (PLGA, PLA) through **nanoprecipitation technique** modifying different parameters:

- Volume Ratio between Organic and Aqueous Phase
- Organic Phase (*Acetone/Dimethyl Sulfoxide*)
- Polymer composition (*PLGA, PLGA-PLA*)
- Surfactant type (*Pluronic F68, Tween 80)* and percentage

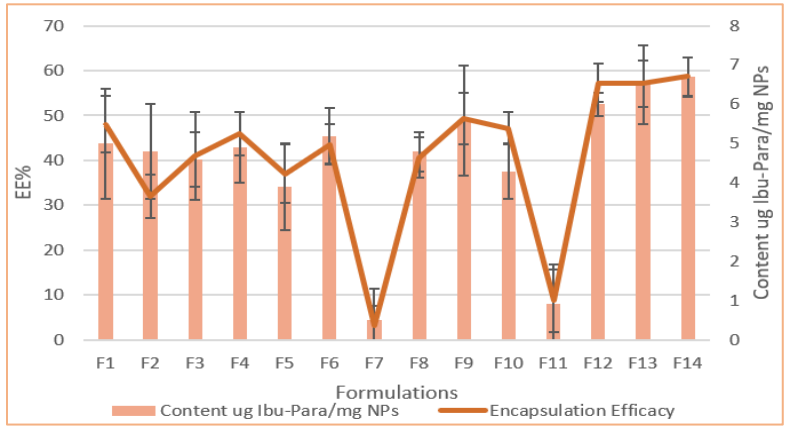


Scheme 5. Chemico-physical characterization of IPc NPs

Every Ibuprofen-Paracetamol NPs formulations were characterized in terms of **size (nm), PdI (Polydispersity index) and Zeta-Potential (mV).**

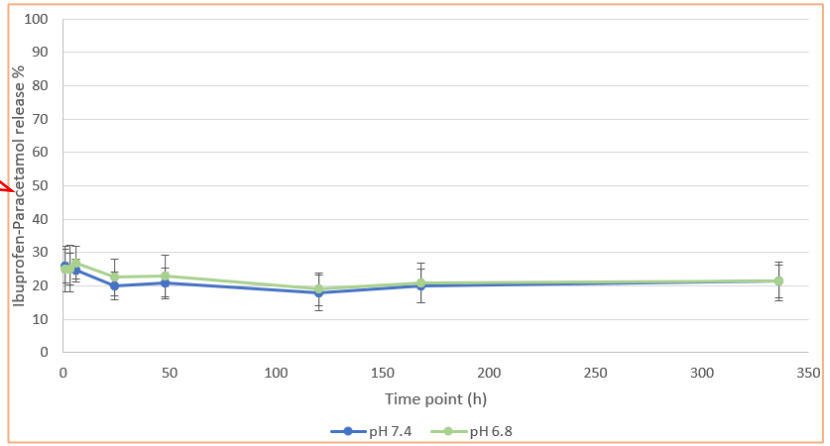
- ***Size:*** 150-200 nm
- ***PDI*** <0.250
- ***Zeta-Potential***: -20 Mv - -40mV

Formulations	Polymers	Organic solutions	Surfactant solution
F1	50 mg PLGA	4 ml Acetone	12,5 ml Pluronic 3%
F2			12,5 ml Pluronic 1.5%
F3			12,5 ml Pluronic 0.5%
F4			25 ml Pluronic 1.5%
F5		1ml DMSO + 3ml Acetone	12,5 ml Pluronic 3%
F6			12,5 ml Pluronic 1.5%
F7			12,5 ml Pluronic 0.5%
F8		5 ml Acetone	12,5 ml Pluronic 3%
F9			12,5 ml Pluronic 1.5%
F10			12,5 ml Pluronic 0.5%
F11			12,5 ml Tween20 1%
F12	PLGA-PLA 50:50		12,5 ml Pluronic 1.5%
F13	75:25 PLA-PLGA		
F14	50mg PLA		



Scheme 6. Pharmaceutical characterization of IPc NPs

NPs based on **PLA**, loaded with **5 mg Ibuprofen-Paracetamol** and prepared using **5ml of acetone** as organic solution and **12,5ml of Pluronic 1,5%** as surfactant solution have proven to be the best formulation.



Scheme 7. Release study of IPc NPs in buffer PBS pH 7.4 and 6.8

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Thanks for the attention

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