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pharmaceutics
MDPI

LIPID-BASED NANOCARRIERS FOR ROSE BENGAL DERMAL DELIVERY: A PROMISING APPROACH IN MELANOMA TREATMENT

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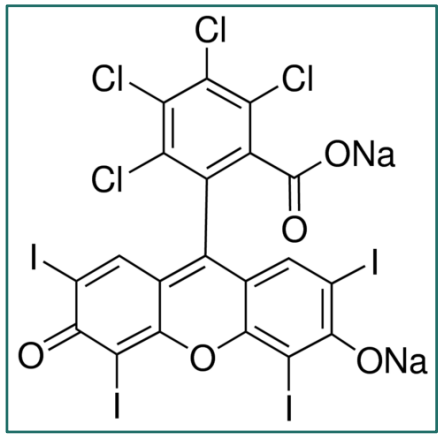
Rose Bengal disodium salt (RB)

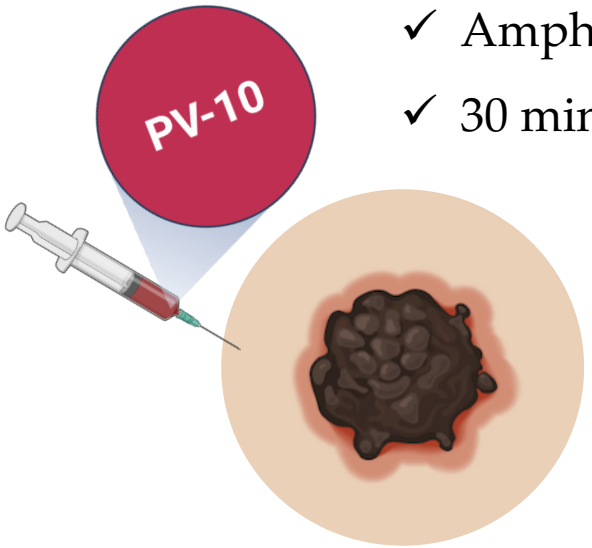


- ✓ Photosensitizer / sonosensitizer drug
- ✓ Ophtalmic diagnostics
- ✓ Antimicrobial agent
- ✓ Cancer therapy

BIOPHARMACEUTICAL PROFILE

- ✓ 1017.64 g/mol molecular weight
- ✓ Water-soluble drug
- ✓ Amphiphilic molecule
- ✓ 30 minutes half-life

PV-10 ®
intralesional injection



Intrinsic melanoma toxicity

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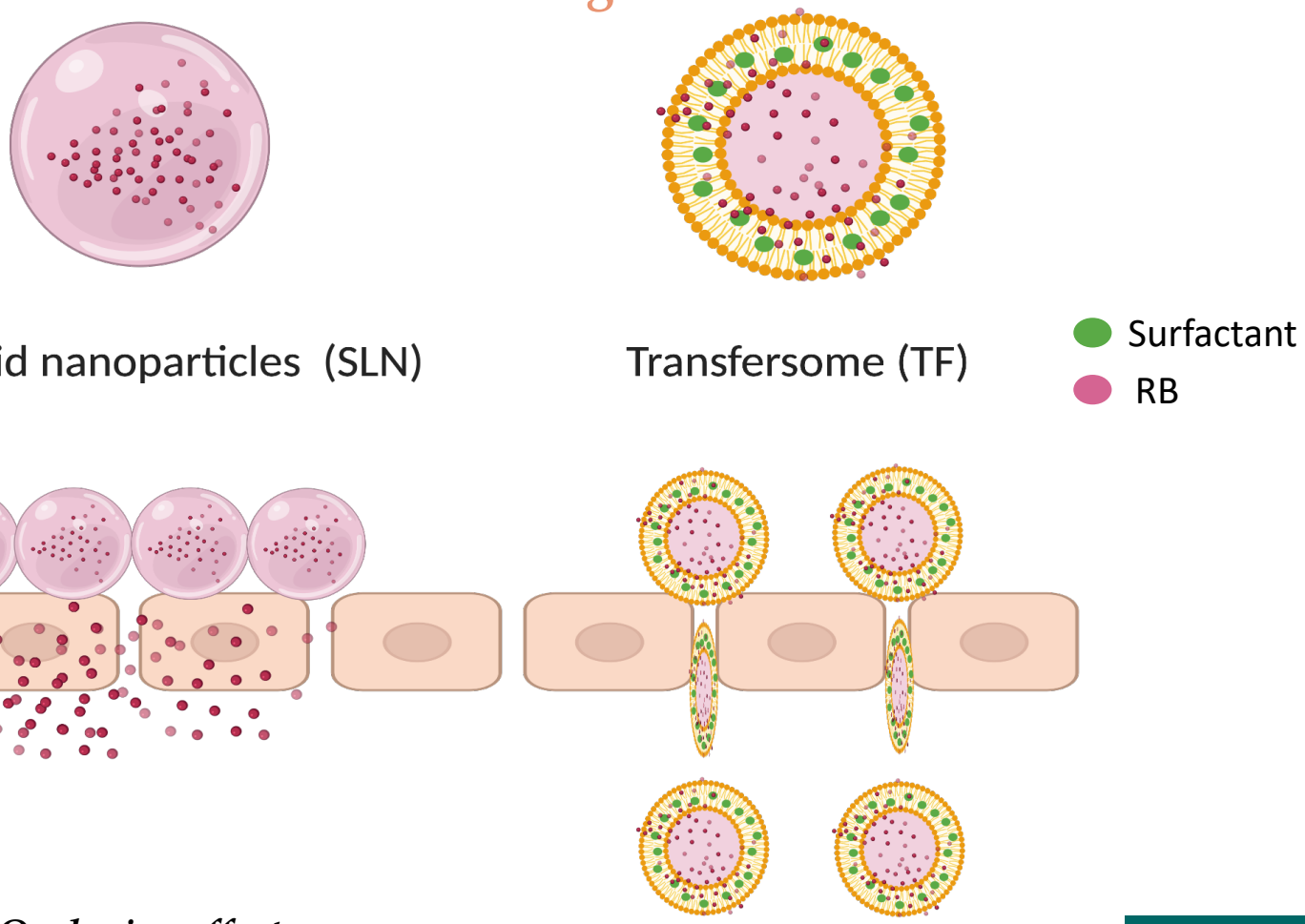
Development of RB loaded lipid nanocarriers for melanoma therapy in the absence of light



***1. Occlusive effect*:**
Enhanced drug penetration,
controlled drug release.
2. Affinity for lipid skin.

***Ultradeformability*:**
drug release in the deepest
region of the body.

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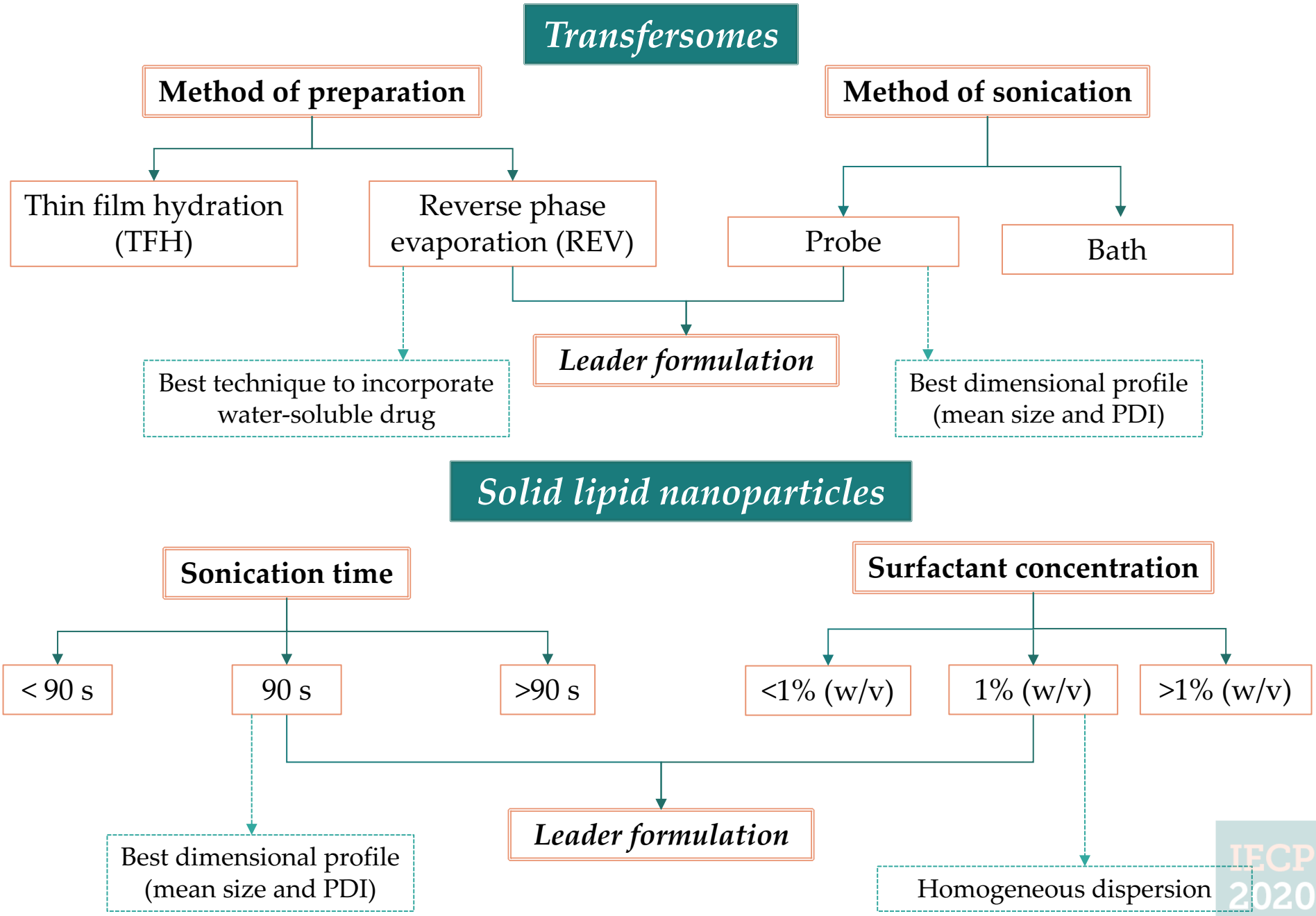
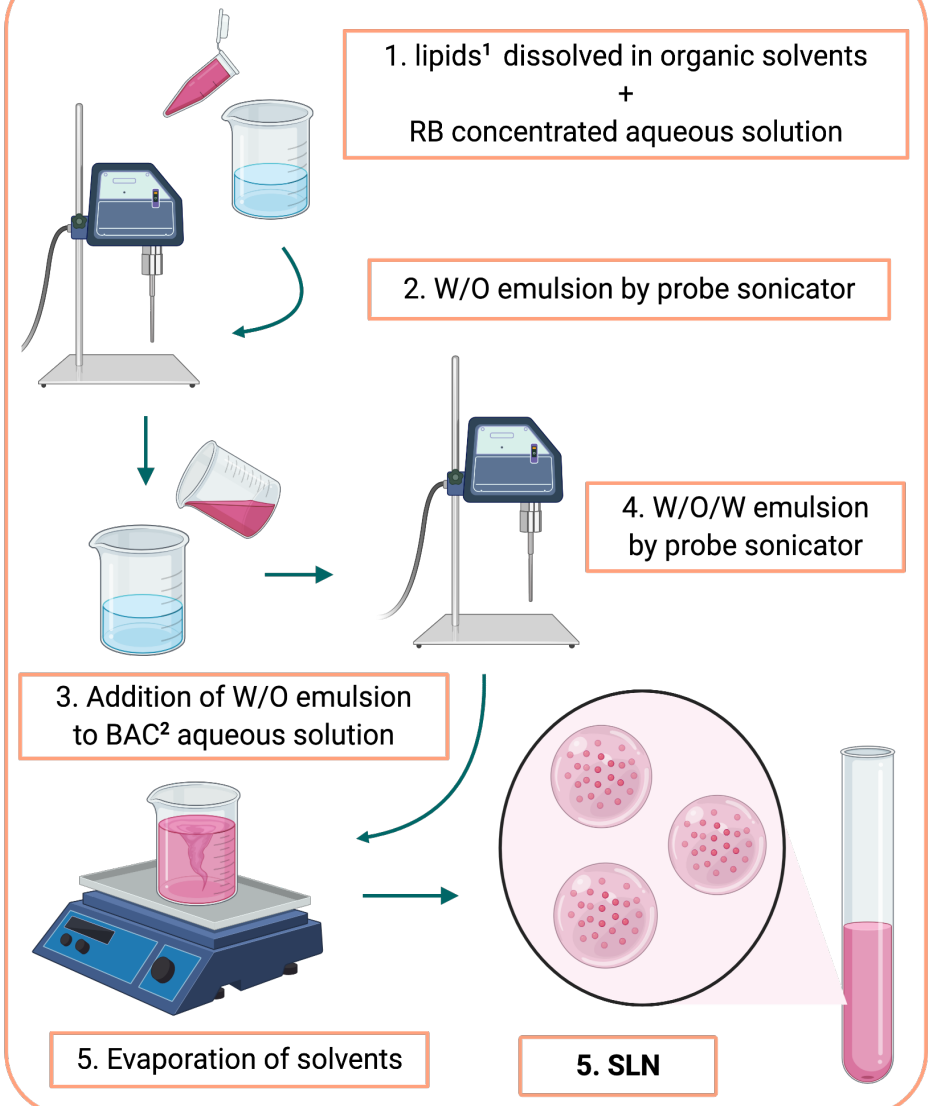
Preformulative studies



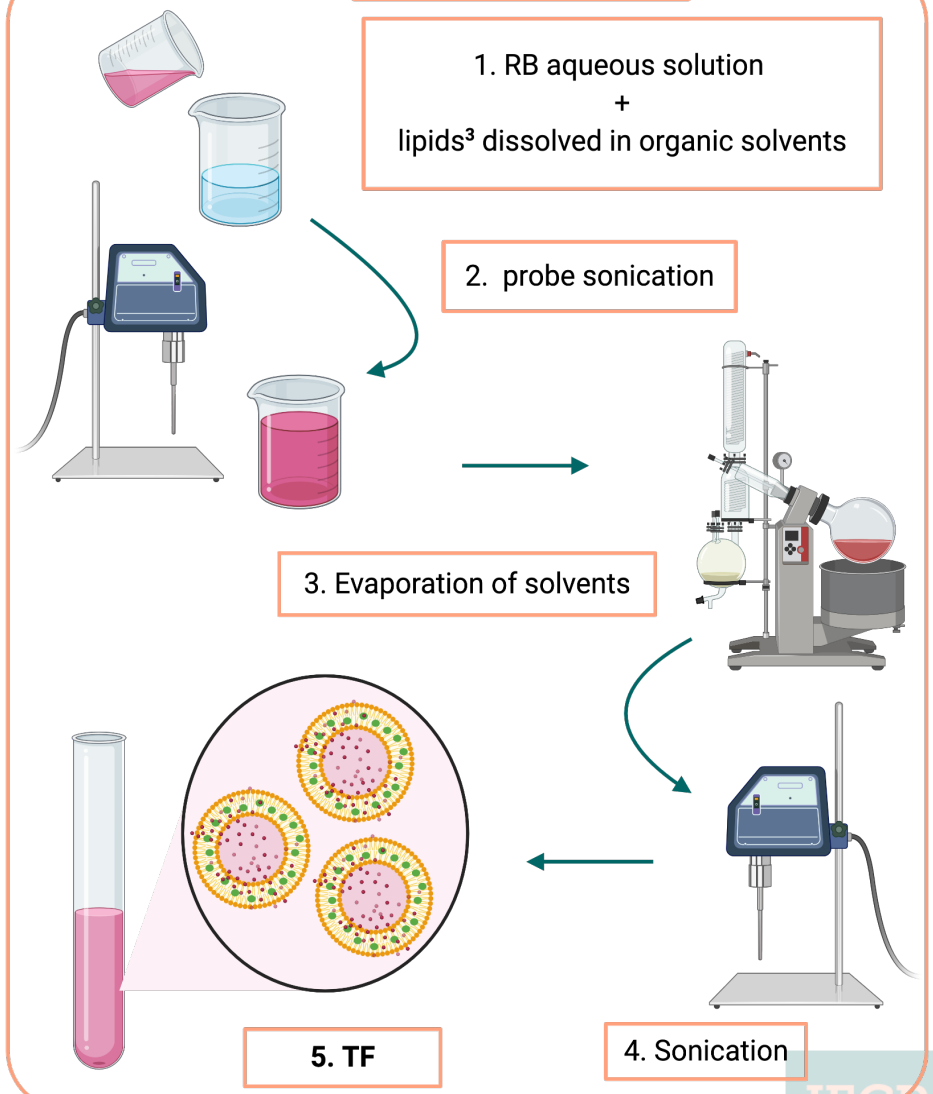
NANOCARRIERS METHOD OF PREPARATION

RB LOADED (200 µM and 500 µM) SLN AND TF WERE PREPARED:

SLN (W/O/W method)

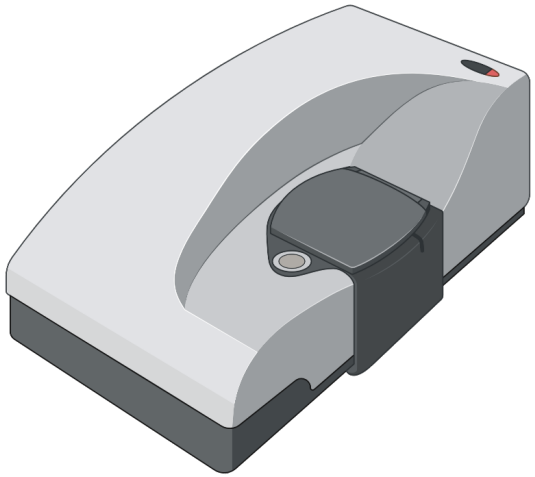


TF (REV method)



[1] Witepsol® E85, Gelucire® 44/14; [2]Benzalkonium chloride; [3]Lipoid S100, cholesterol, Span® 80

Results and discussions: DIMENSIONAL PROFILE AND ZETA POTENTIAL



Coulter nanosizer

Formulation	Particle Size (nm±SD)	PDI (±SD)	Zeta potential (mV)
SLN blank	130.1±3.01	0.225±0.02	61.2±2.4
SLNRB-200	133.0±3.19	0.231±0.01	64.5±1.1
SLNRB-500	135.4±03.35	0.220±0.01	63.5±1.5
TF blank	219.11±1.79	0.23±0.09	-4.9±0.9
TFRB-200	202.77±2.06	0.28±0.01	-26.0±0.2
TFRB-500	230.67±1.02	0.20±0.02	-48.7±0.4

- ✓ Nanocarriers were in a dimensional range that enhances skin penetration of photosensitizer drugs[1].
- ✓ Zeta potential (ζ) values are such as to avoid nanoparticles aggregation (ζ<30 mV; ζ>60 mV)[2].

[1]Md, S et al; Lipid based nanocarriers system for topical delivery of photosensitizers. *Drug Discov. Today* **2017**, *22*, 1274–1283, doi:10.1016/j.drudis.2017.04.010.

[2]Zahra Hadian et al; Formulation, characterization and optimization of liposomes containing eicosapentaenoic and docosahexaenoic acids; a methodology approach. *Iran. J. Pharm. Res. IJPR* **2014**, *13*, 393–404.

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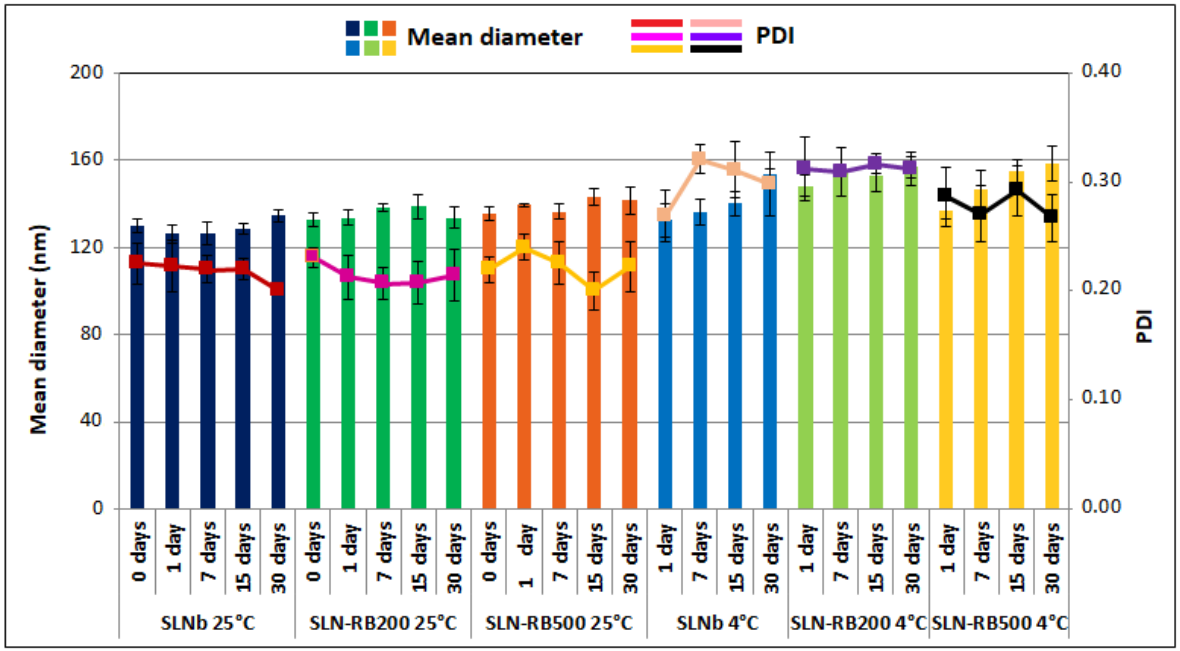
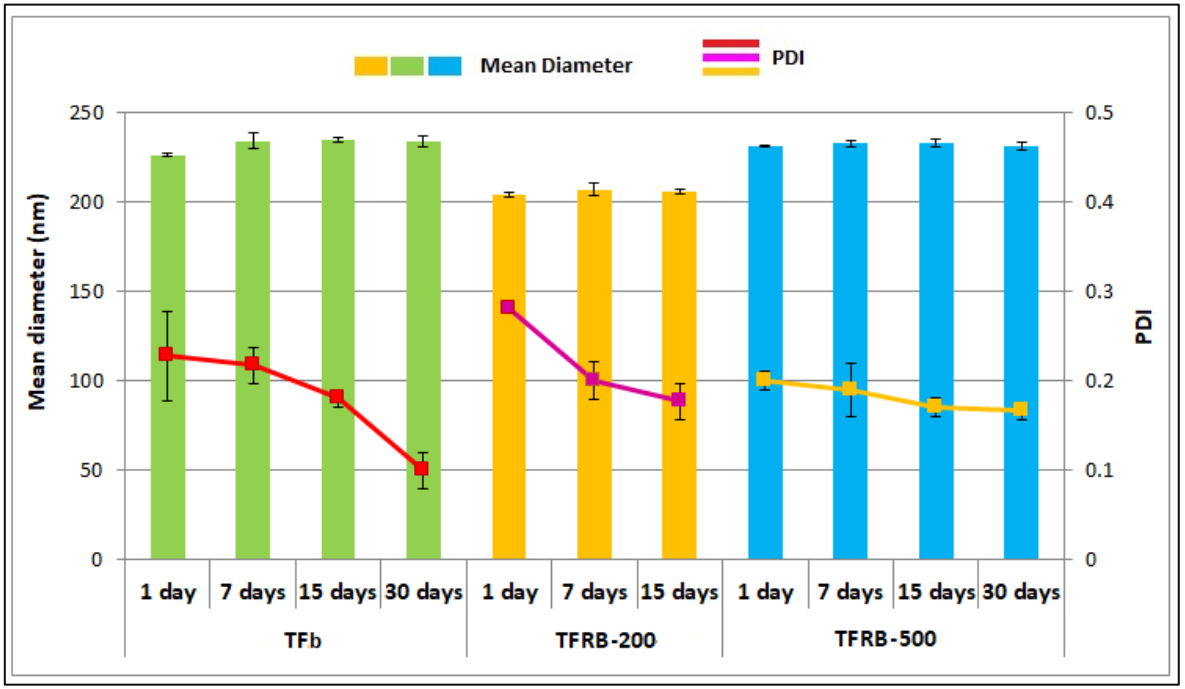
Results and discussions: PHYSICAL STABILITY





Nanocarriers demonstrated to be stable after one month of storage.

- ✓ SLN were stable at 25°C
- ✓ TF were stable at 4°C

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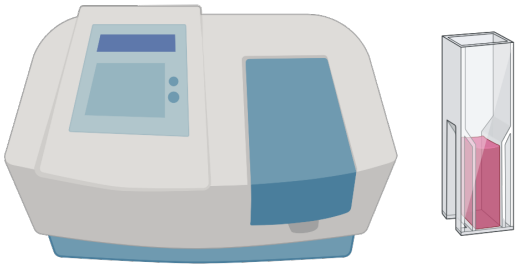
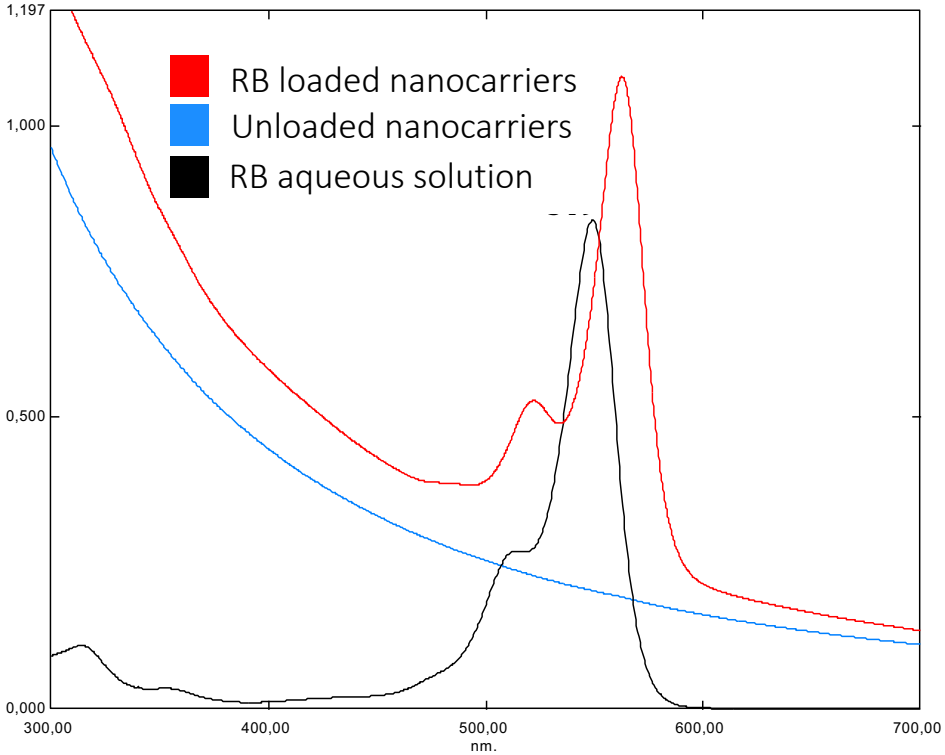
Results and discussions: RB INTERACTION WITH NANOCARRIERS



UV-spectrophotometer; spectrofluorometer

Formulation	Abs (nm)	Ems (nm)
RB	549	568
SLNRB-200	565	581
SLNRB-500	564.5	582
TFRB-200	562	582
TFRB-500	562.5	583



Absorption spectra of formulations

RB maximum absorption and emission wavelength red-shifted when RB is formulated in nanocarriers compared to water[3].

✓ RB bounded to lipid components of SLN and TF

[3]Hugo E. et al; Effect of temperature on the photobehavior of Rose Bengal associated with dipalmitoylphosphatidyl choline liposomes, J. Lumin. 131 (2011) 2468–2472.

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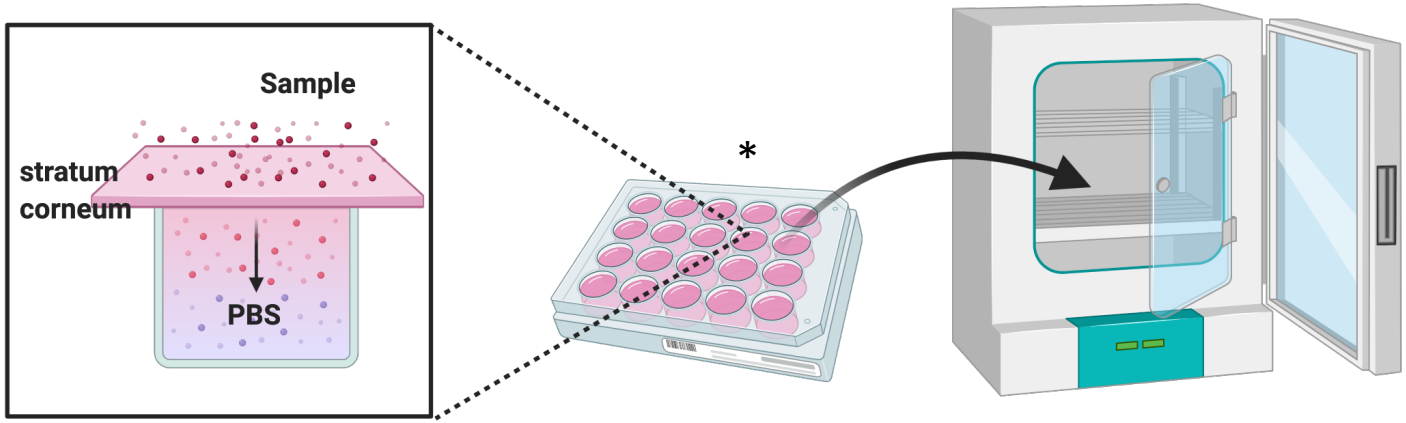
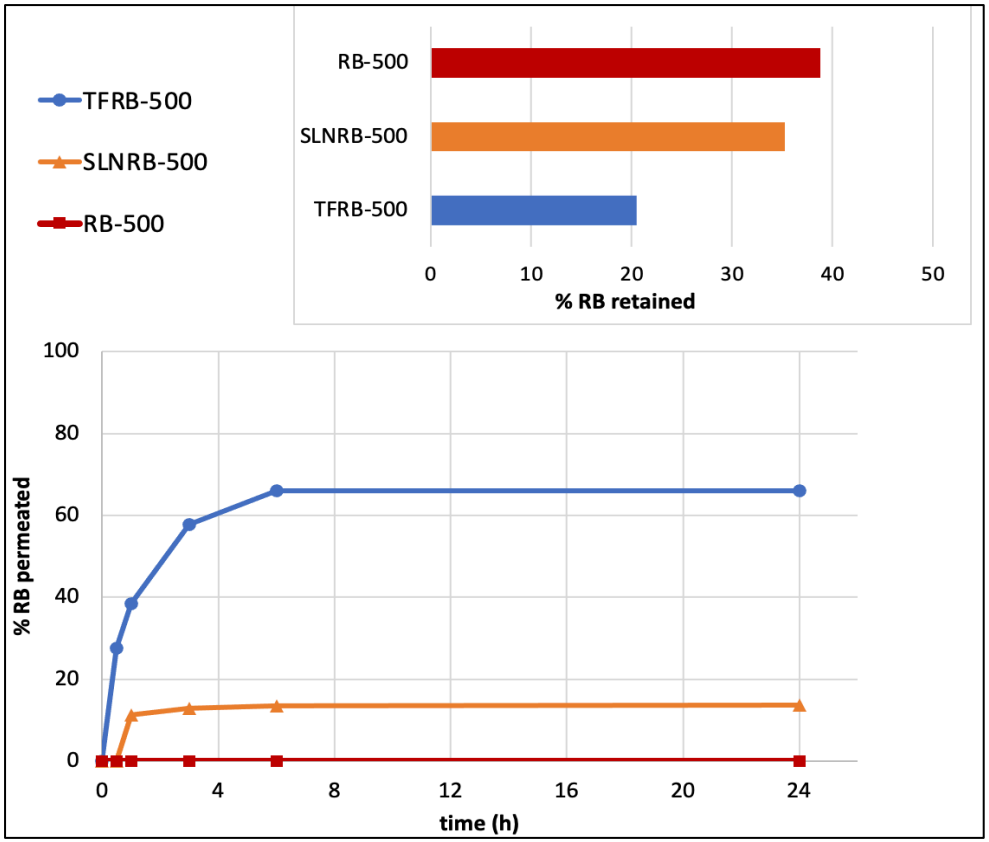
Results and discussions: PRELIMINARY EX-VIVO PERMEATION STUDY



** project INCREASE SARDINIA 2016-17, protocol number 31351, University of Sassari*

30 min, 1h, 3h, 6h, 24h



- ✓ Free RB did not permeate according to its chemical profile and a part of it was retained by stratum corneum
- ✓ TF increased RB permeation as they can squeeze along the intracellular lipid of stratum corneum.
- ✓ SLN slightly increased RB permeation but most of them were tissue-retained prolonging RB interaction with stratum corneum and enhancing its penetration into the deepest layers.

- ✓ Nanocarriers were in a dimensional range suitable for topical delivery and they are stable after one month.
- ✓ SLN and TF proved to interact with RB.
- ✓ The preliminary permeation study reported that TF permeated through stratum corneum and they could be employed to reach melanoma cells.
- ✓ SLN were mainly found within stratum corneum so they could be considered to treat skin disease involving stratum corneum itself, with the advantage of protecting RB from undesirable light activation.
- ✓ Cytotoxicity studies on melanoma cells are ongoing, and further physical-chemical characterizations are planned

Acknowledgements

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uniss
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Thanks for your attention!