# Light-activated drug release from liposome-hydrogel systems

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Tampere University

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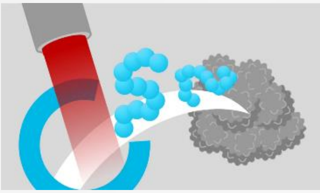
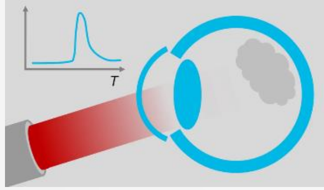
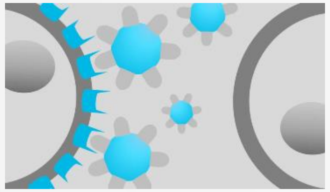
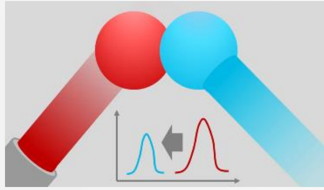
# PHARMACEUTICAL NANOTECHNOLOGY

(https://www.helsinki.fi/en/researchgroups/pharmaceutical-nanotechnology)









## Light activation and photochemistry

- Light activated liposomes
- Part of the **PREIN Flagship**

## Nanoparticles for drug delivery

- Liposomes, micelles, DNA nanoparticles etc.
- Part of the **GeneCellNano Flagship**

## Hydrogels and controlled drug release

- Cellulose nanofibers (Collaboration with UPM)
- Photoactivatable Drug Releasing Implants (**ERC Consolidator Grant**)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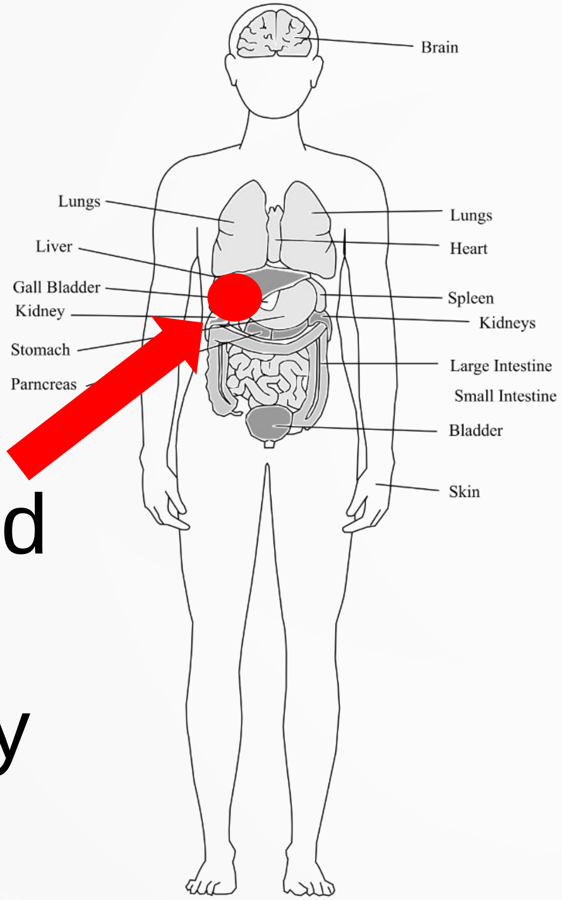
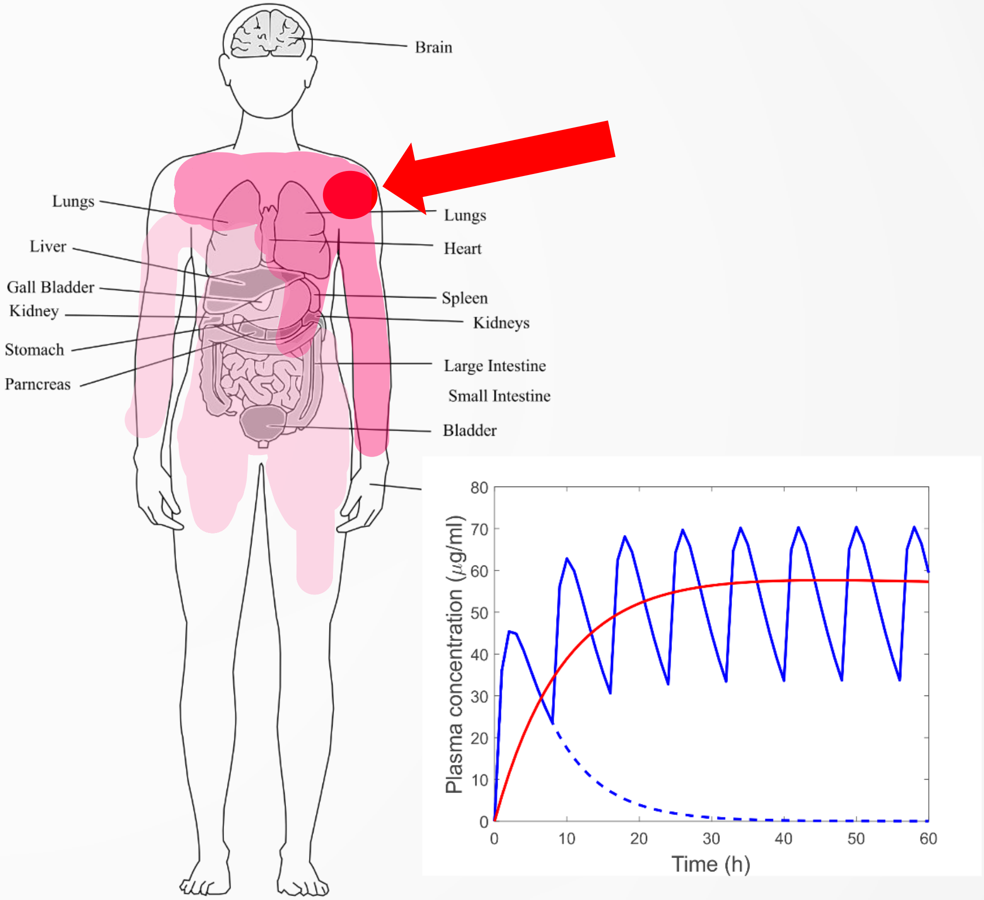
# PARTICLES IN CIRCULATION VS. CONTROLLED DRUG RELEASE MATERIALS




Targeted drug delivery




Controlled release

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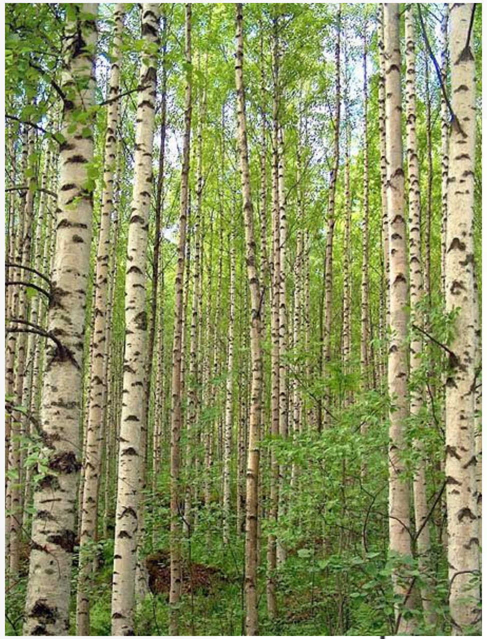
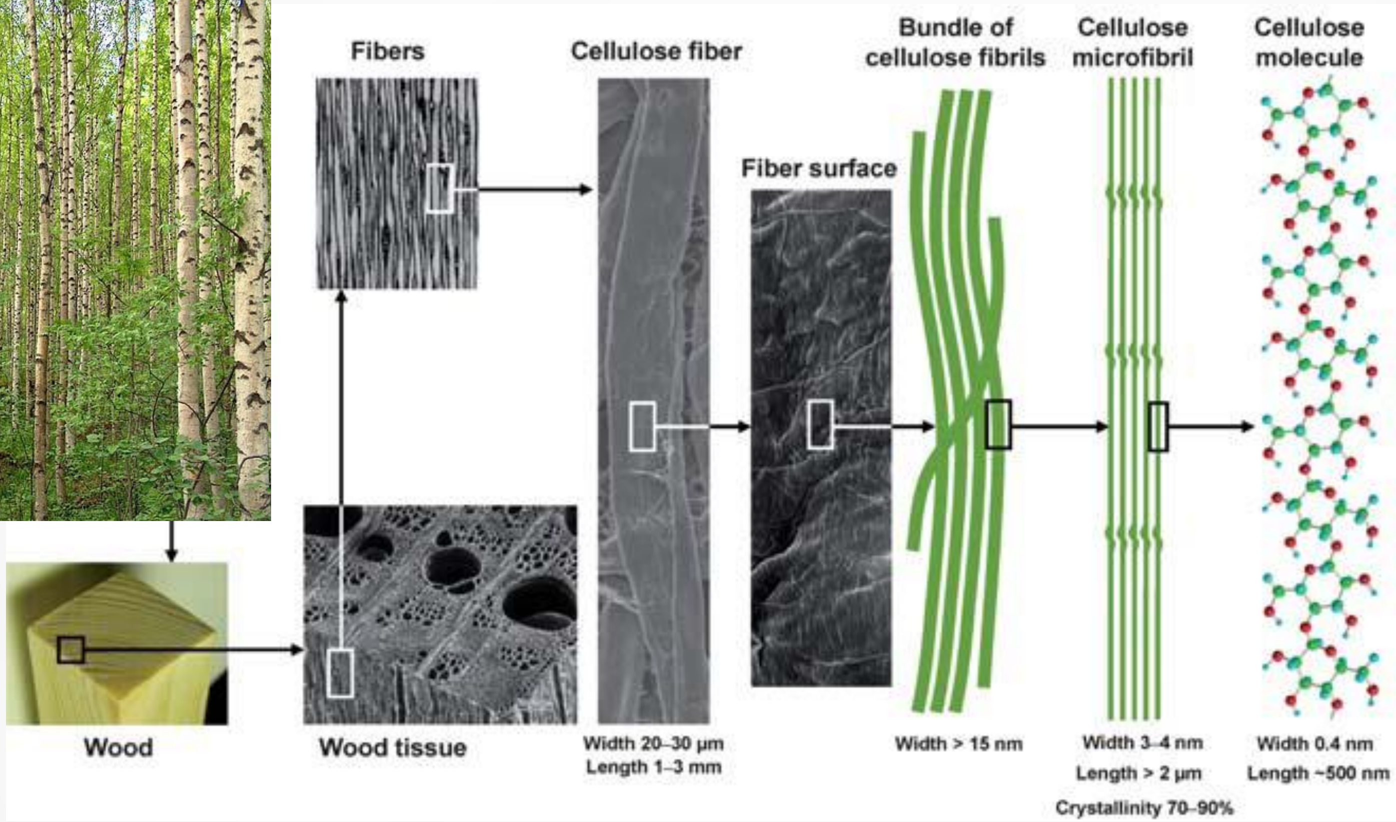
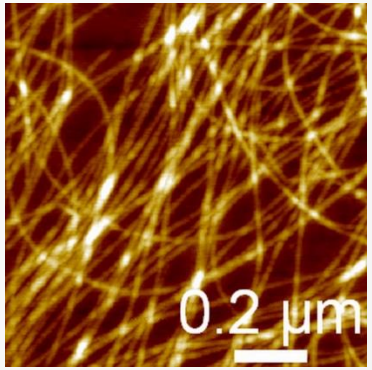
# CELLULOSE NANOFIBERS (NFC/CNF)



Hierarchical structure of wood biomass and the characteristics of cellulose microfibrils

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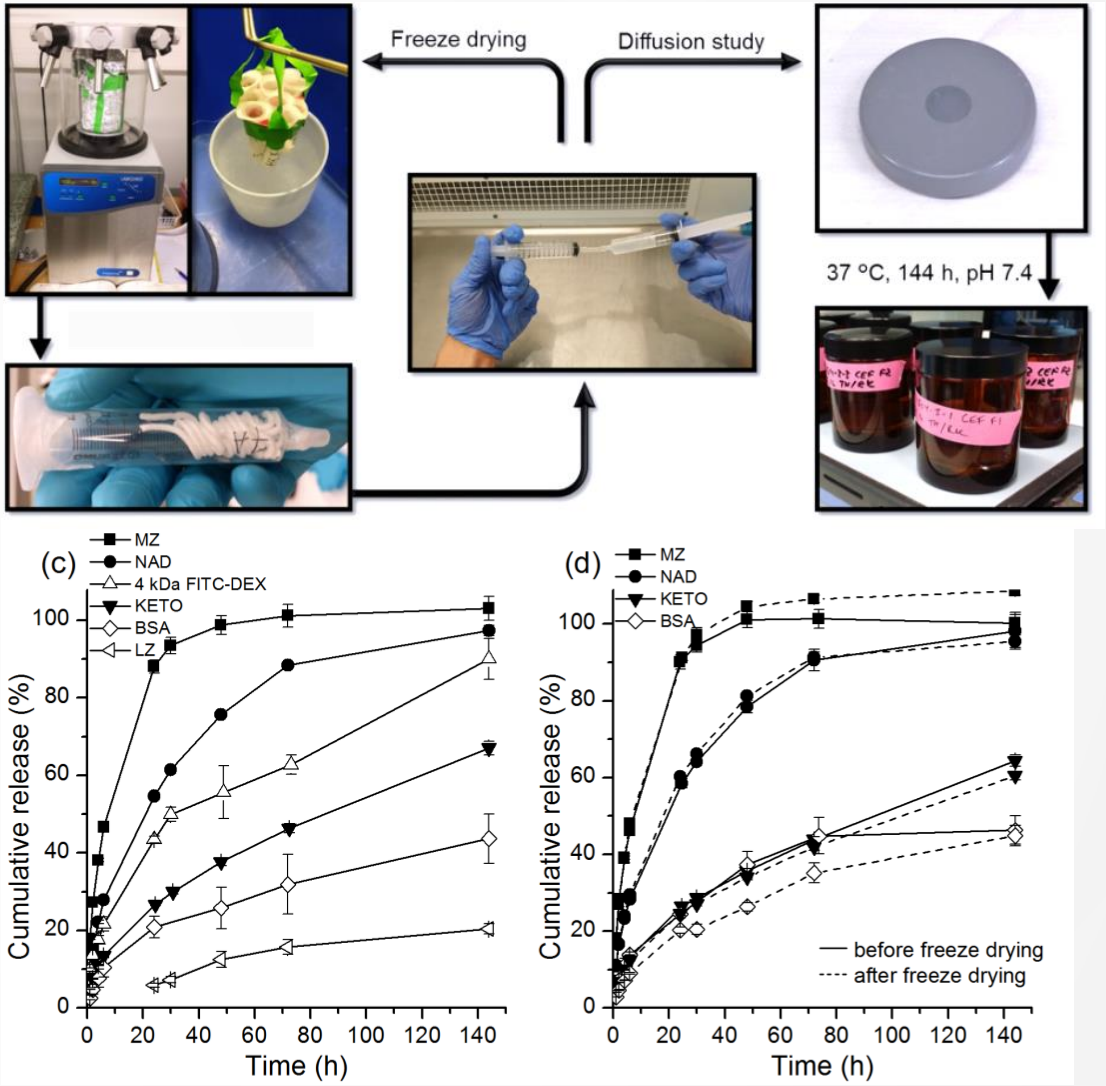
Adapted from Isogai et al., Nanoscale, 2011
Valo et al., Eur. J. Pharm. Sci., 2013

# HYDROGELS AS DRUG RESERVOIRS

**Using the hydrogel directly – more convenient approach**

- Cellulose nanofiber hydrogel as a starting material (native / oxidized)
- Sustained drug release possible
- Hydrogels can be freeze-dried and rehydrated for improved storage
- APIs can be successfully incorporated and diffusion coefficients determined

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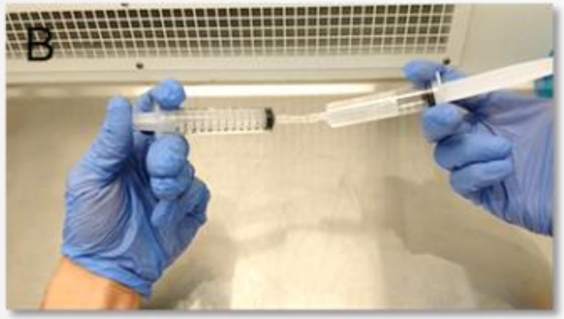
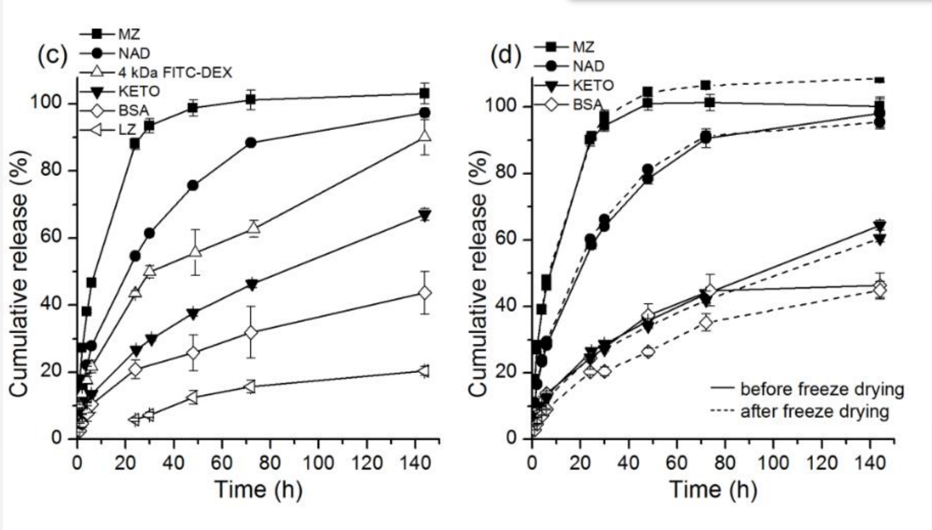
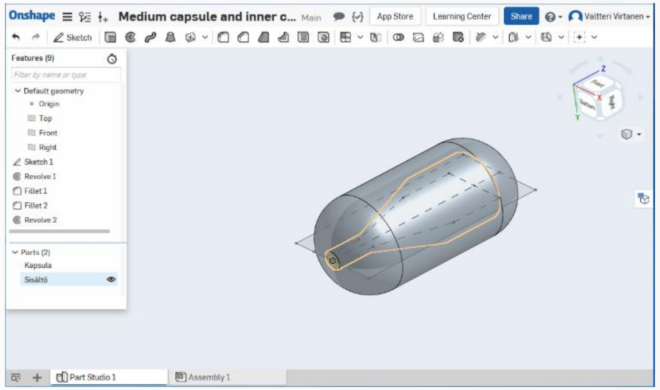
Paukkonen, H., et al., Int. J. Pharm, 2017

# HOW TO BETTER CONTROL OR MODULATE THE RELEASE RATE?

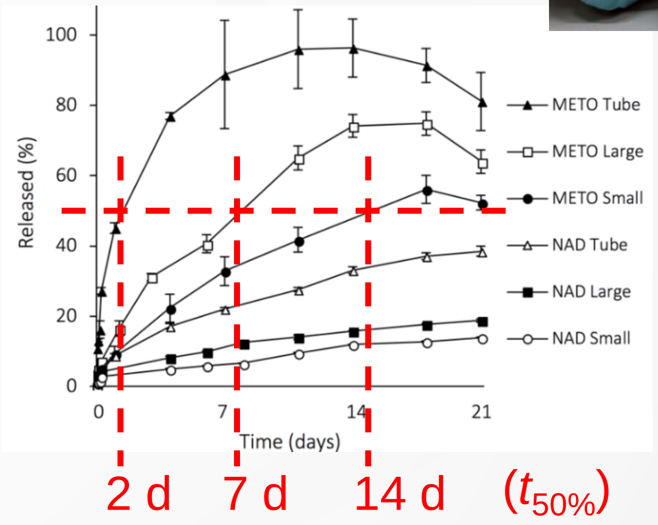






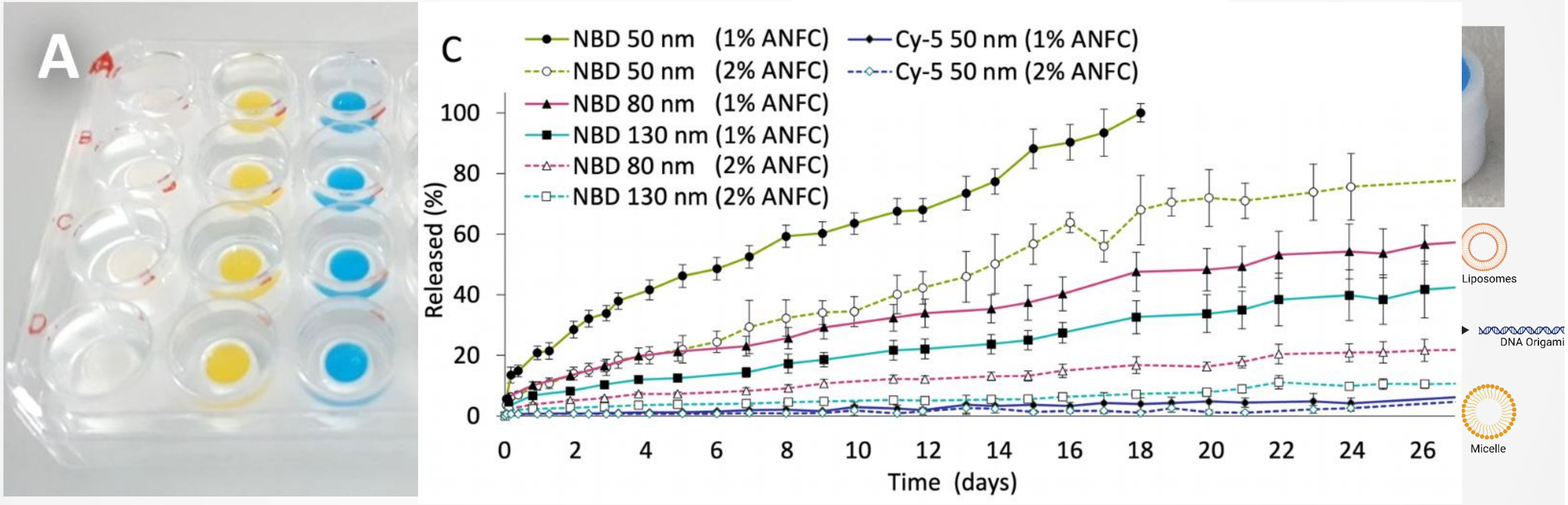





Auvinen, V.-V., et. al, J. Drug Del. Sci. Tech., 2020

# HOW ABOUT BIGGER THINGS, LIKE NANOPARTICLES, INSTEAD OF MOLECULES?




Increasing nanocellulose concentration slows down the release

Positive charge locks the particles inside the hydrogel



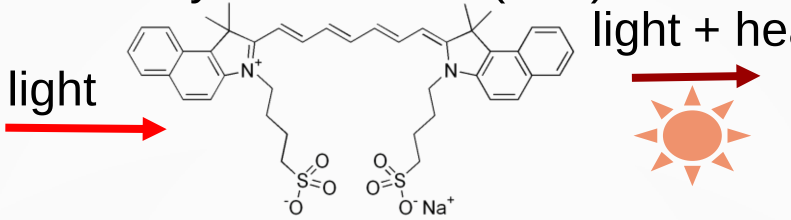
Auvinen, V.-V., et al., Cellulose, 2022

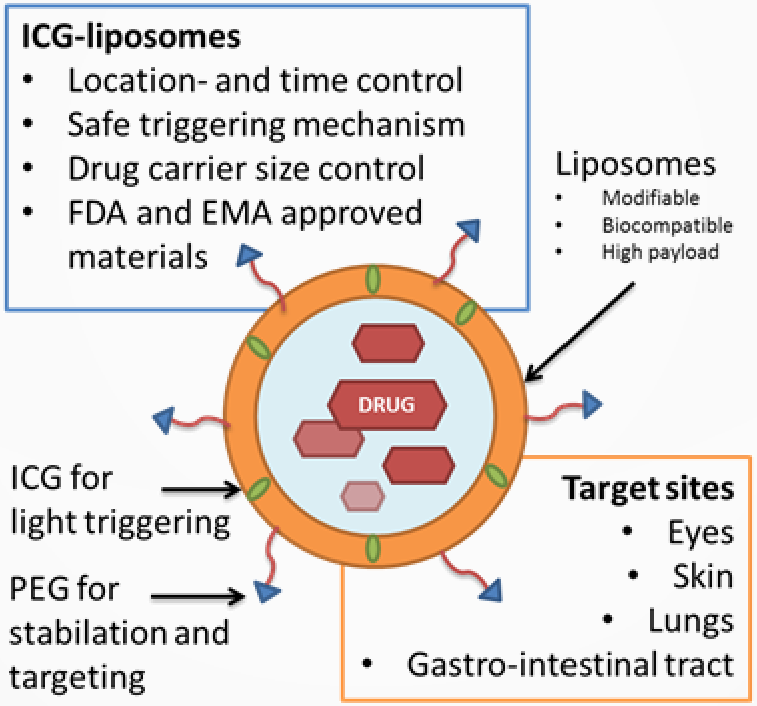
# LIGHT-ACTIVATION OF LIPSOMES

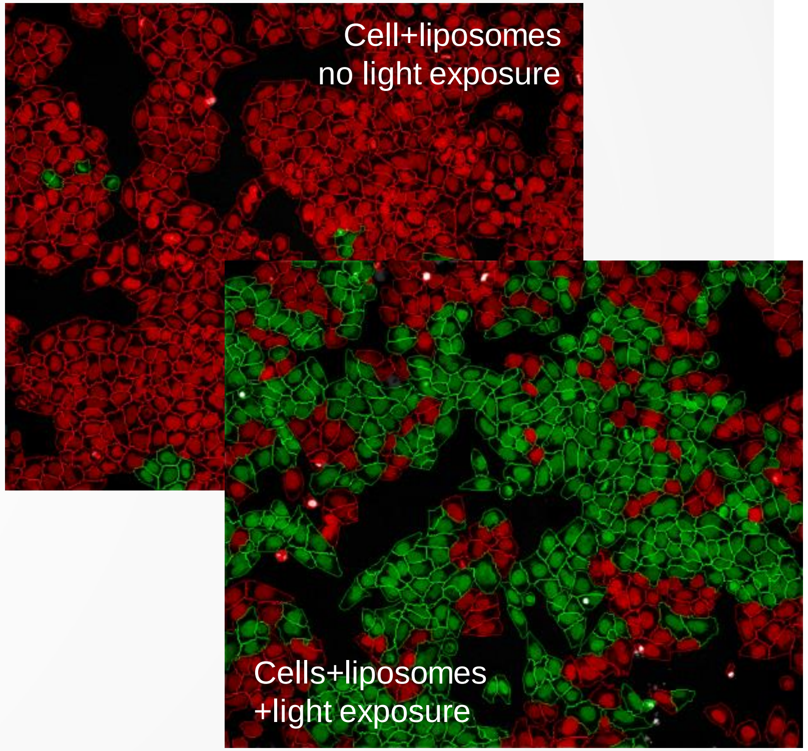
Light excitation at 808 nm enables good tissue penetration and safety

Light energy is converted to heat, which releases the contents from thermosensitive liposomes

Indocyanine Green (ICG)



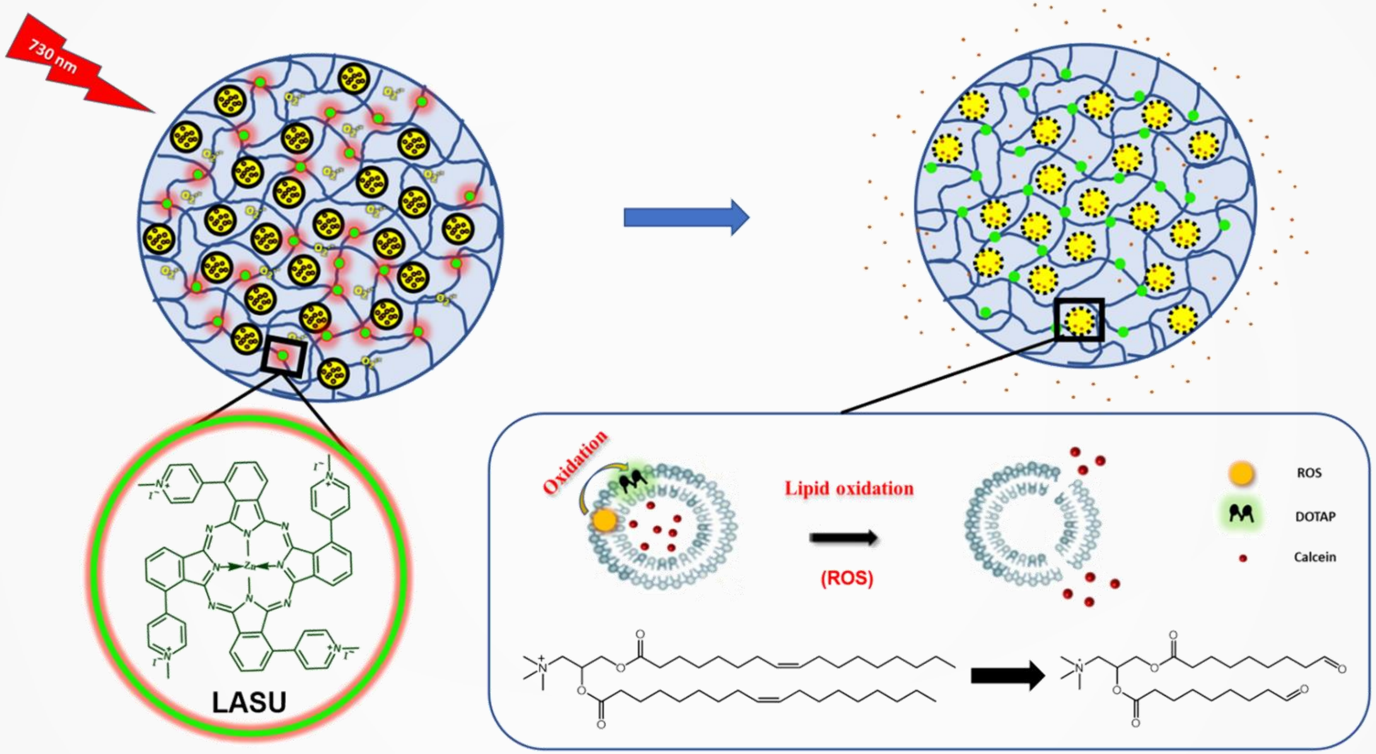




Lajunen, T., et al., Mol Pharm, 2016
Lajunen, T., et al., J. Controlled Rel., 2015
Paasonen, L., J. Controlled Rel., 2007

# PHOTO-OXIDATION – ANOTHER METHOD FOR LIGHT ACTIVATION


Olga Lem




LASU – Zn phtalocyanine photosensitizer for ROS generation. Binds to cellulose!
Liposomes also bind to cellulose → Simple mixing is enough to process the material

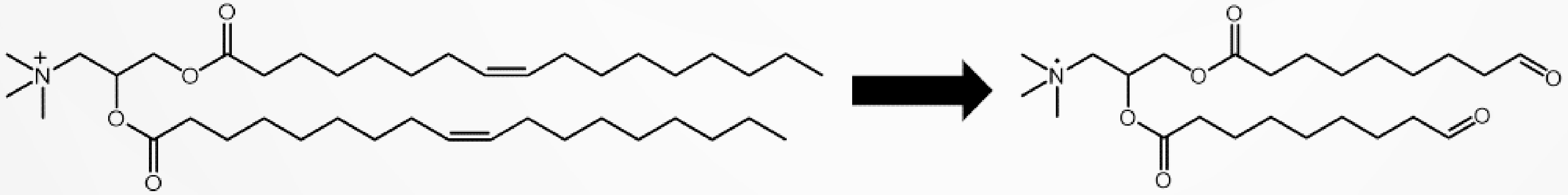


Lem et al., Carbohydr. Polym. 2024

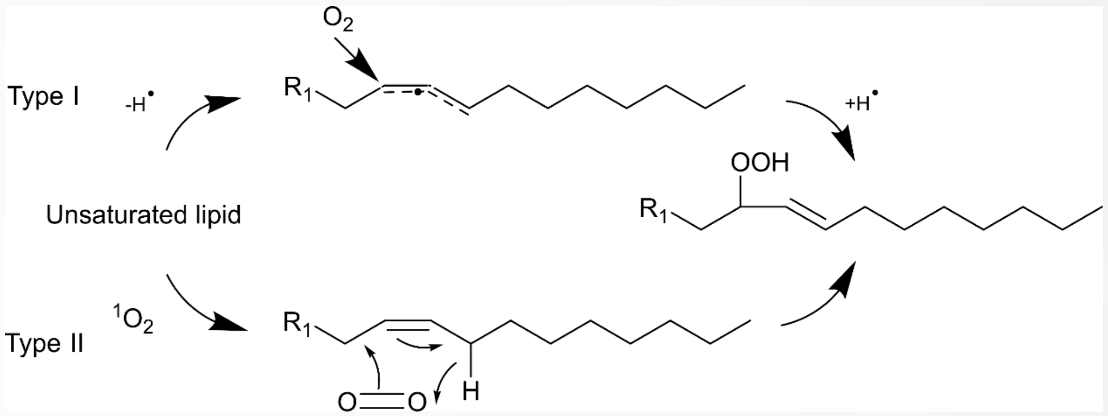
# LIPOSOMES AND ROS - SIMPLER

Optimization is considerably easier, for example this works:

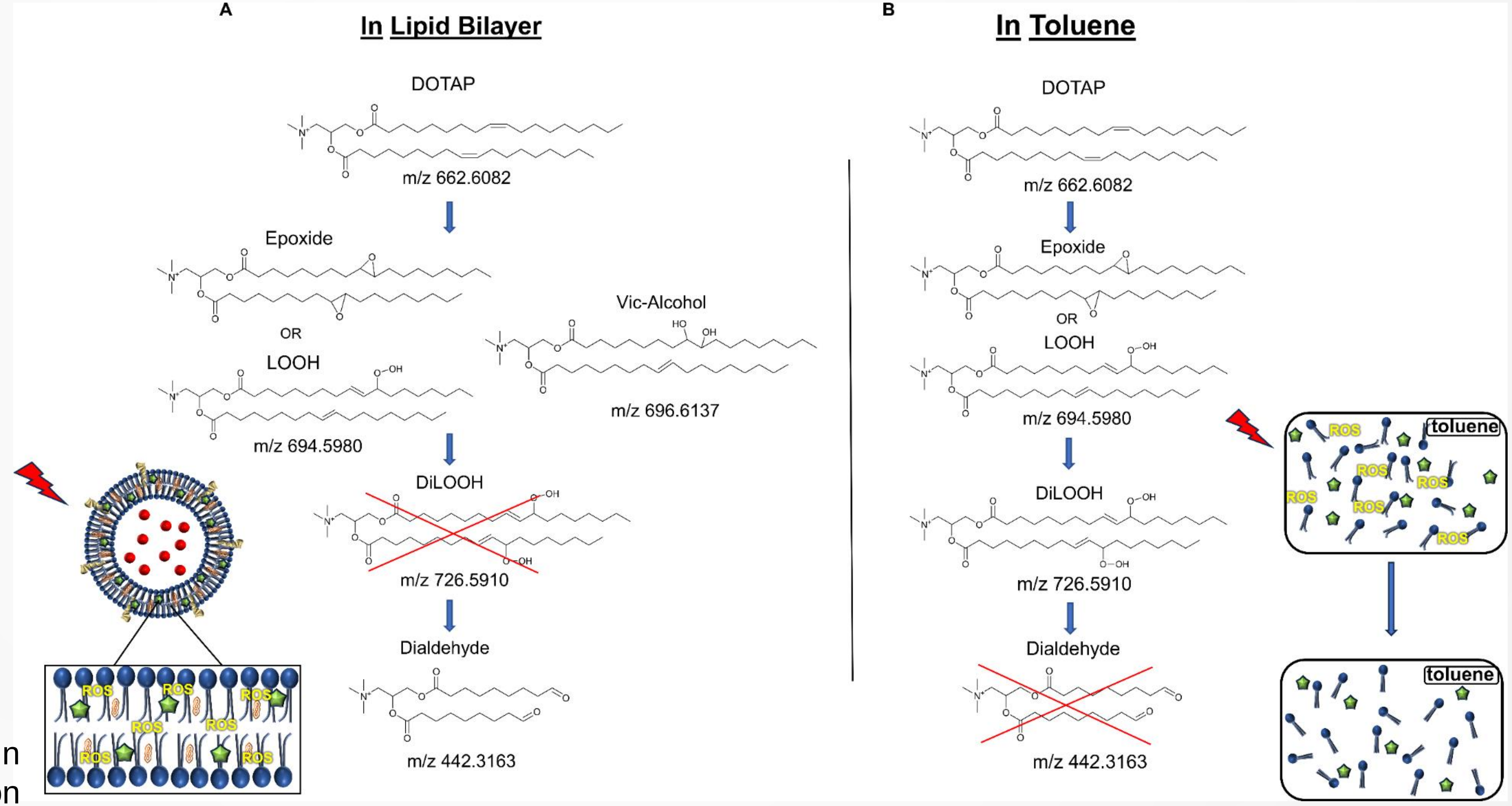
| | | |
|---|---|---|
| 60% | DPPC | Stability, prevents leakage |
| 30% | DOPC/DOTAP | **ROS-sensitivity** |
| 5% | DSPE-PEG | Biocompatibility |
| 5% | Cholesterol | Stability, prevents leakage |



# LIPID OXIDATION




Free radicals or singlet oxygen lead to the oxidation of lipids (hydroperoxides)




In practice, several different oxidation products are seen (related to the applied light dose)

Manuscript in preparation

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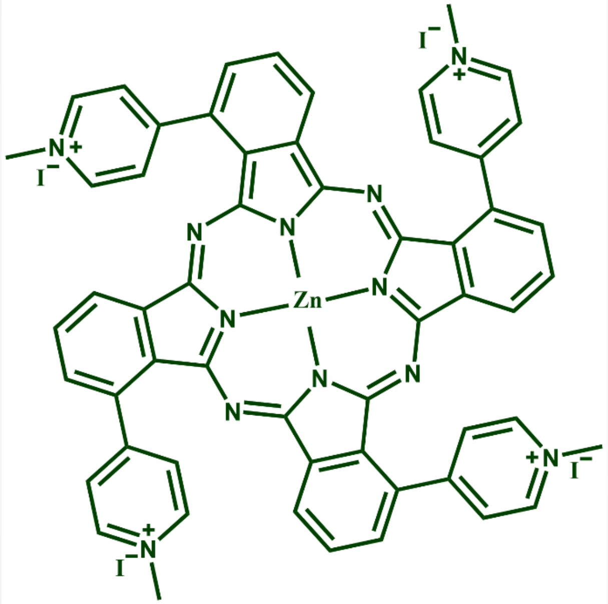
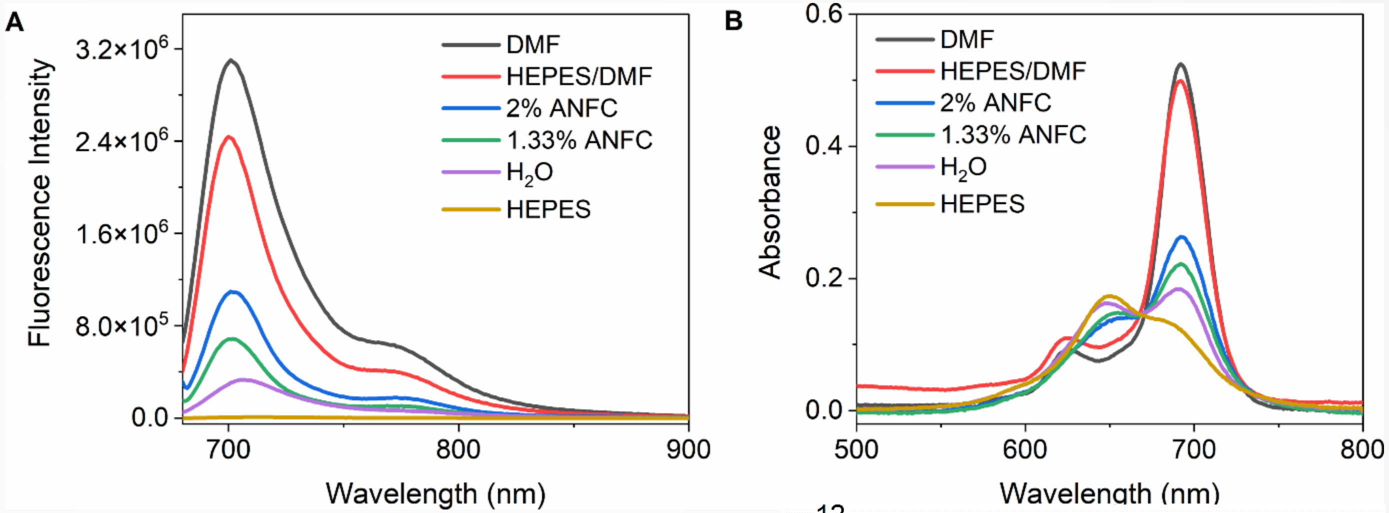
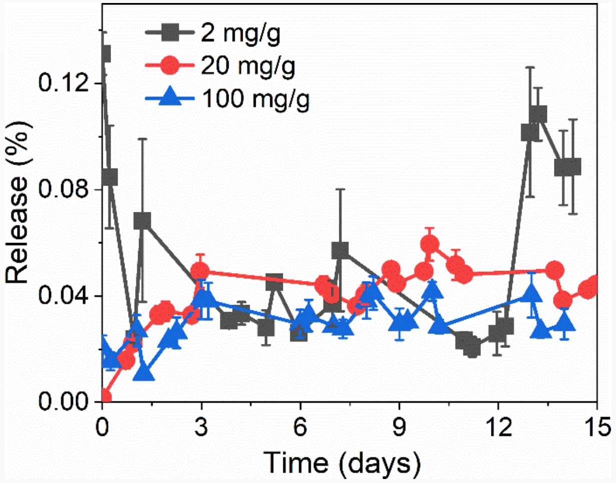
# RED-LIGHT ABSORBING SENSITIZER BINDS TO CELLULOSE



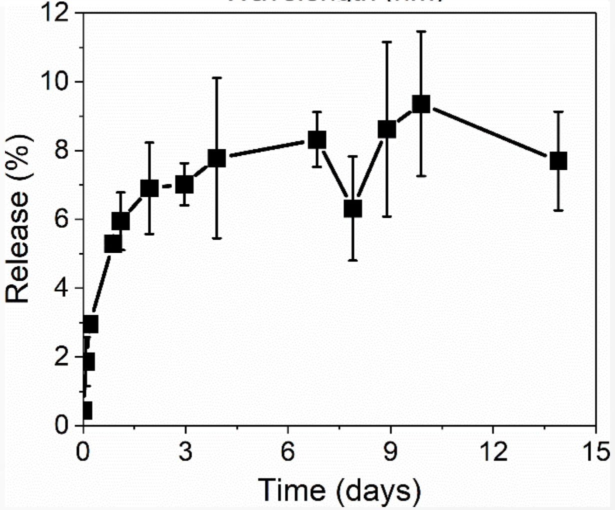
Pyridine substituted phthalocyanine zinc complex

Absorption max. at ca. 690 nm




No release of the dye from CNF




No release of the liposomes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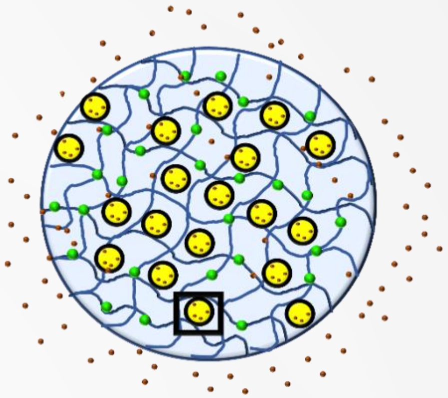
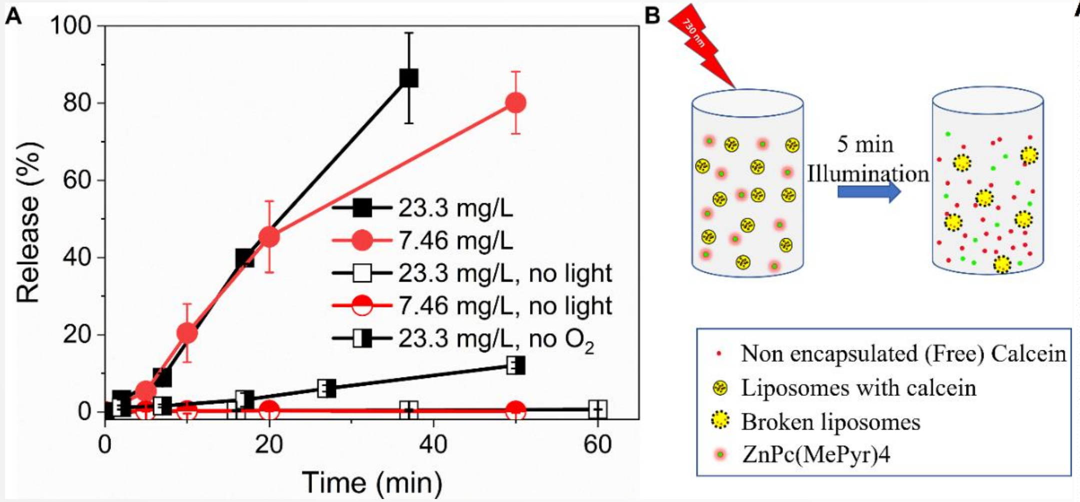
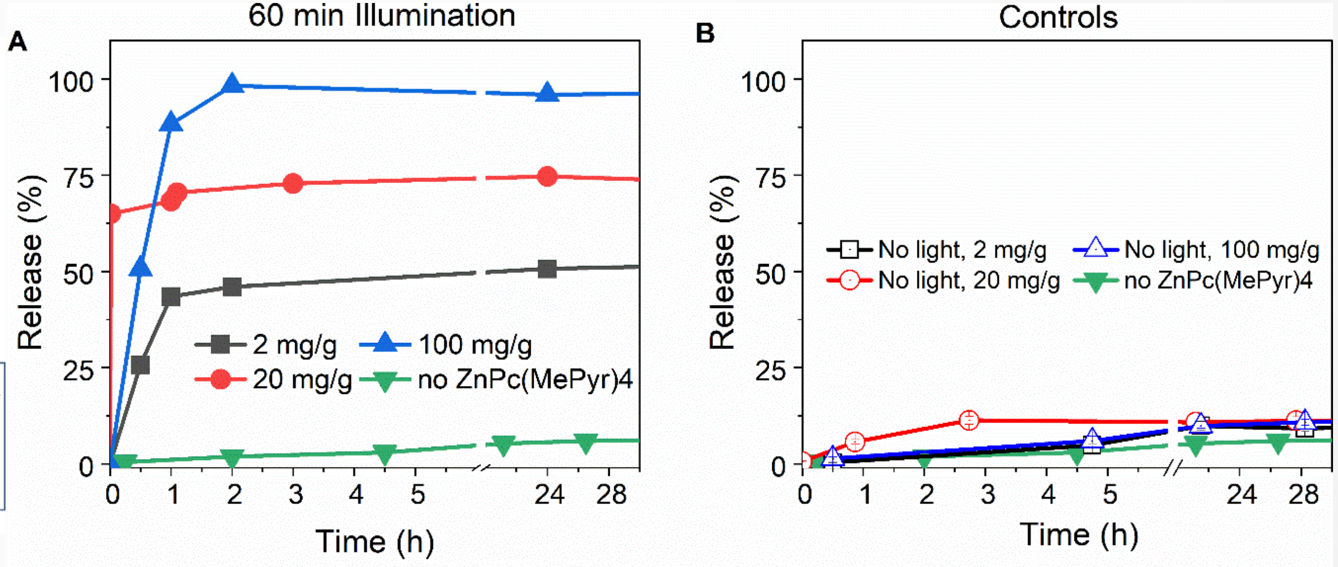
# LIGHT-ACTIVATED & ROS-MEDIATED RELEASE FROM CELLULOSE NANOFIBERS



## Release from the liposomes




## Release from CNF






Lem et al., Carbohydr. Polym. 2024

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