Porphyrin free organic contrast agents for photoacoustic imaging

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Background

Exogenous contrast agents not only allow to further enhance the quality of the obtained images, but also, when combined with biomarkers, provides the tools to visualize biological processes in the body. Gold nanoparticles are the most common contrast agent, but their biocompatibility is limited as their accumulation causes oxidative stress and may lead to permanent cellular damage.

In this work, we asses the photacoustic (PA) response of porphyrin-free covalent organic framework nanoparticles (nCOFs) as novel exogenous contrast agents for PA imaging. These nanostructures are 100% organic, biodegradable, present strong stability in physiological fluids, and are non-cytotoxic in a wide range of concentrations [1, 2].

Methods

Two types of nCOFs have been compared with the standard commercial reference (gold nanoparticles) and with fluorophore ATTO532 loaded on mesoporous silica nanospheres (MSNs). Both comparison nanoparticles have their peak at 532 nm.

Preparation of stable nCOFs (LZU-1 and TAPB-PDA)

For the preparation of 1,3,5-Benzenetricarboxaldehyde (LZU-1) and 1,3,5-Tris(4-aminophenyl)benzene-Terephthaldehyde (TAPB-PDA) nanoparticles, we followed an optimized recipe from refs [3] and [1] respectively. Both nCOFs have their absorption peak around 250 nm.

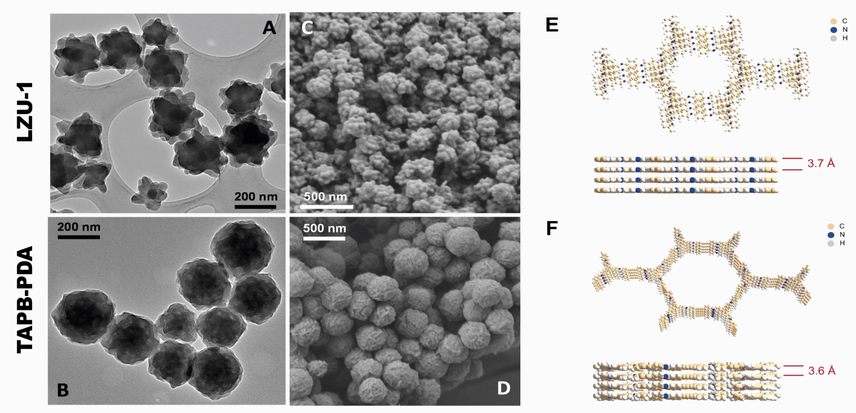


Fig 1. Characterization of LZU-1 and TAPB-PDA nCOFs. (A-B) TEM images. (C-D) FESEM images. (E-F) Simulated 2D eclipsed layered-sheet arrangement indicating the interlayer space.

nCOFs validation as PA contrast agents

The feasibility of the 2D-π conjugated materials LZU-1 and TAPB-PDA, as exogenous contrast for PA imaging, has been analysed using a hybrid US and PA imaging system. The hybrid image allows us to define the inner region of the excited tube containing the nanoparticles, where the PA signal is eventually integrated.

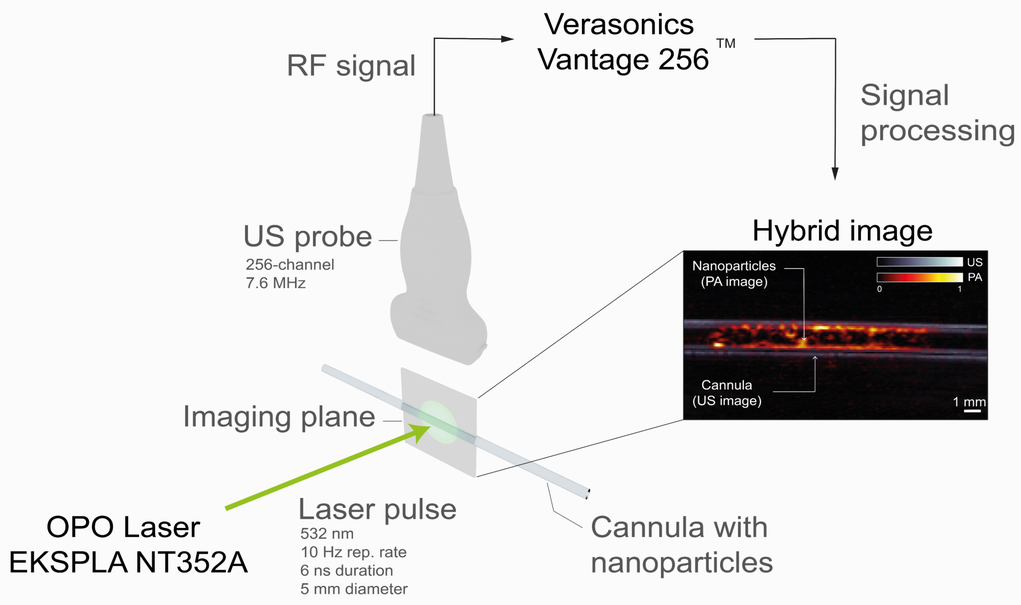


Fig 2. Hybrid US-PAT system. Schematic diagram of the experimental setup.

Results

Nanoparticles samples at low concentration

As expected, gold nanoparticles and MSN-ATTO532 have good response, because their maximum absorption is at the selected laser wavelength.

Interestingly, TAPB-PDA and LZU-1 materials also present significant PA signal amplitude. These could be explained by the imine COFs strong π- π interaction among the layers, which enables absorption along a wide wavelength range and release vibrational energy to produce the PA signal.

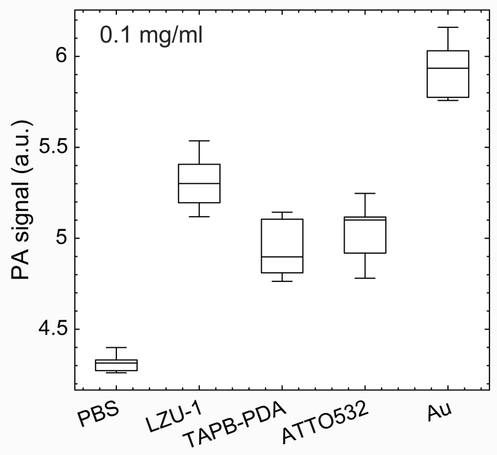
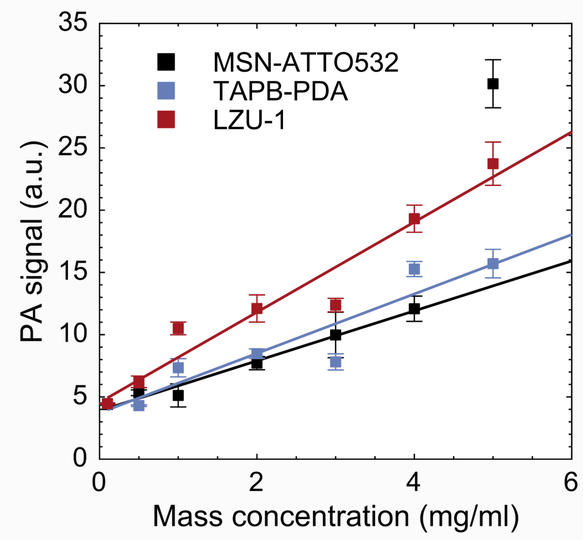


Fig 3. PA response of the PBS (baseline), nCOFs (LZU-1 and TAPB-PDA) and references (MSN-ATTO532 and Au nanoparticles)

Nanoparticles PA response at higher concentration

The advantage of nCOFs is that we could increase the administered concentration, as they are not cytotoxic. We have evaluated the PA response at increasing concentrations. A total of 24 replicates per sample were measured and averaged for each concentration.



The response increases linearly with concentration, exceeding the gold reference at 0.1 mg/ml.

The experimental response fits the theoretical linear approximation with R-square values of 0.98, 0.88 and 0.94 for MSN-ATTO532, TAPB-PDA and LZU-1 respectively.

Fig 4. PA response for increasing nanoparticles concentration obtained experimentally (square markers) and fitted using a linearized model.

Conclusion

Both nCOFs show promising behaviour based on the interlayer stacking of their 2D-structure. As they are organic network structures, it is expected that their concentration can be increased, improving the PA response until the desired contrast is achieved, without causing cell damage.

Besides being biocompatible, non-cytotoxic and non-harmful exogenous contrasts, nCOFs could be loaded with drugs and act as carriers for medical treatments. This would allow them to be both diagnostic and therapeutic agents at once.

References

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