Oxidation Responsiveness of Polythioacetals and their Anti-Inflammatory Potential

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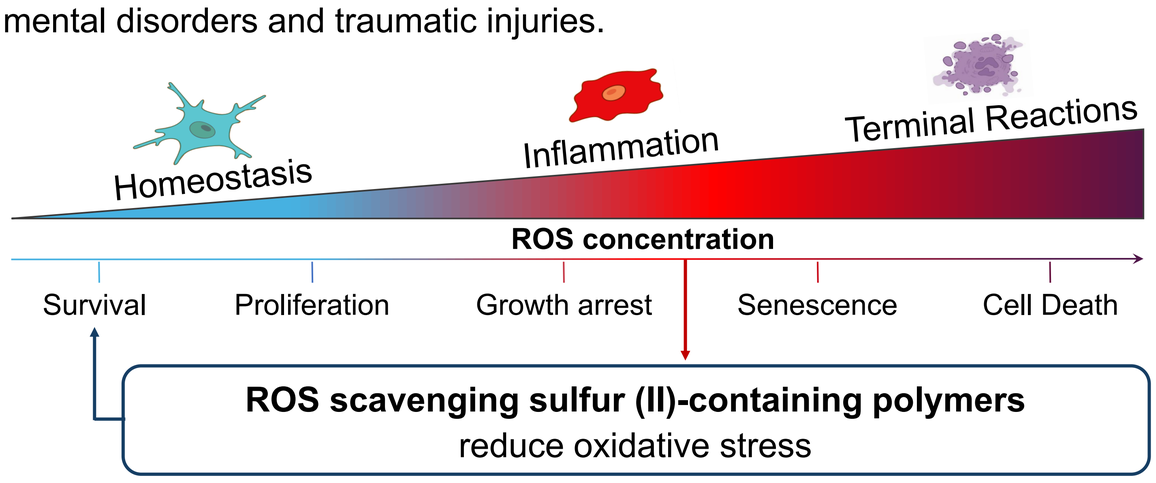
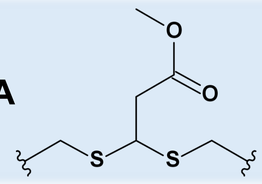
Background

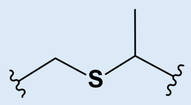
In biology, most oxidants are known as **Reactive Oxygen Species** (ROS) and have markedly different concentration-dependent roles. What occurs in the presence of pathologically high levels of ROS is typically referred to as **oxidative stress**. In the **central nervous system** (CNS), oxidative stress contributes to the onset and progression of neurodegenerative diseases, mental disorders and traumatic injuries.



Poly(thioacetal) **PTA**



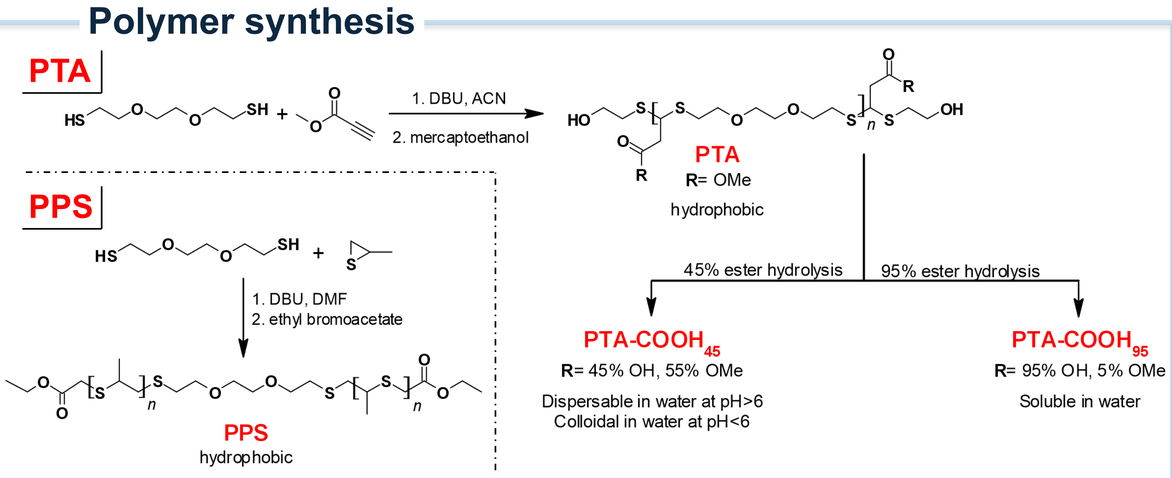
Poly(thioether) **PPS**



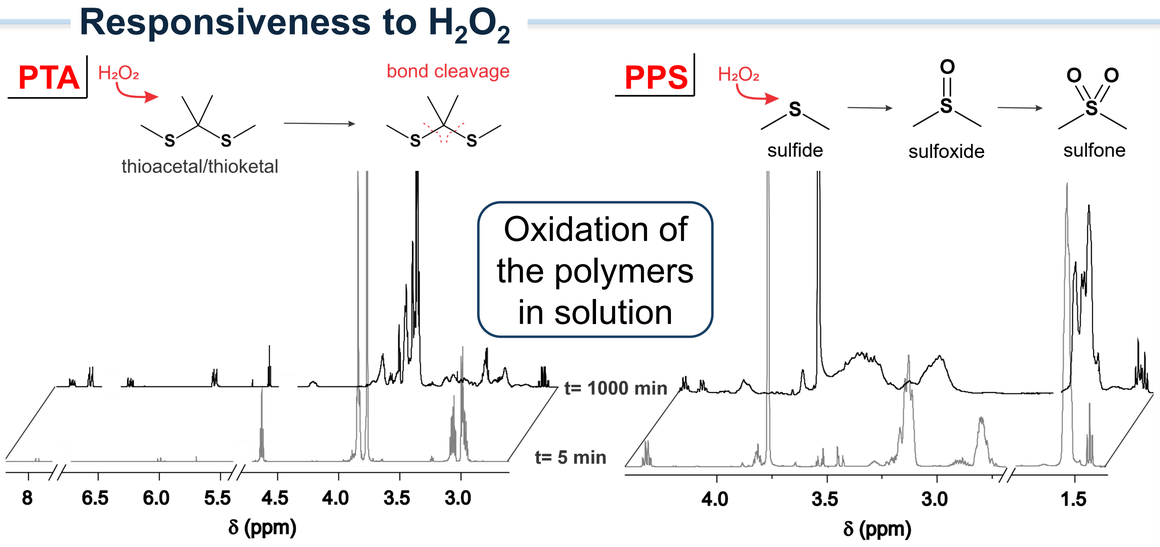
Poly(thioacetal) vs poly(thioether)

Poly(1,3-dithio-6,9-dioxo-2-methylacetate-decane) (**PTA**) and poly(propylenesulfide) (**PPS**) were synthesized, and their ROS scavenging capacity was compared both in a H_2O/THF homogeneous solution and in the form of pluronic-stabilized nanodroplets in phosphate buffer.

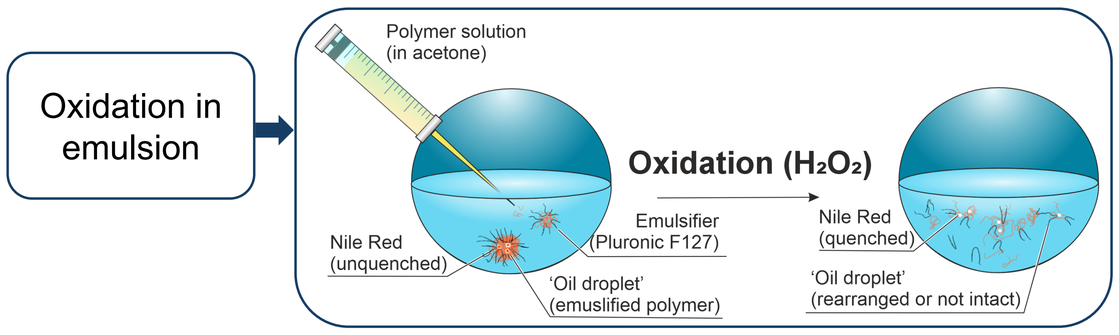
Polymer synthesis

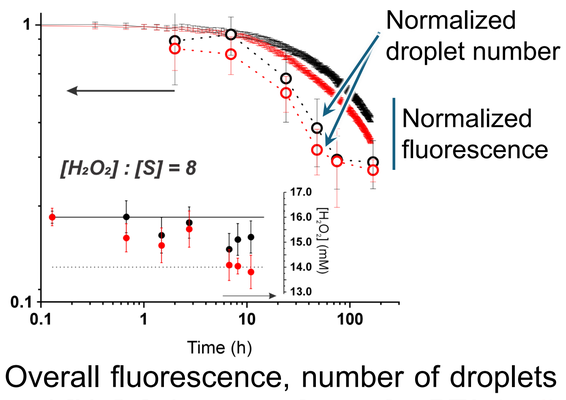


Responsiveness to H_2O_2



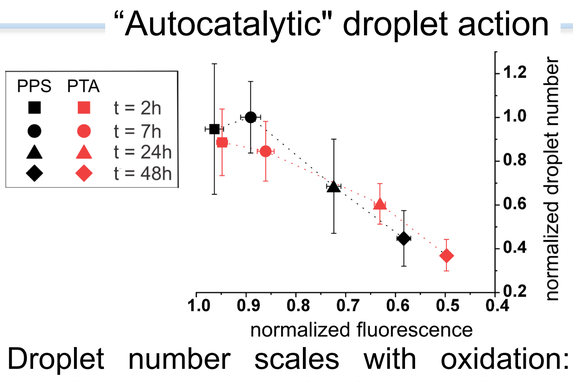
PTA undergoes depolymerization, PPS only increases its hydrophylicity.





Overall fluorescence, number of droplets and $[H_2O_2]$ decrease faster for PTA (red) than PPS (**black**).

"Autocatalytic" droplet action

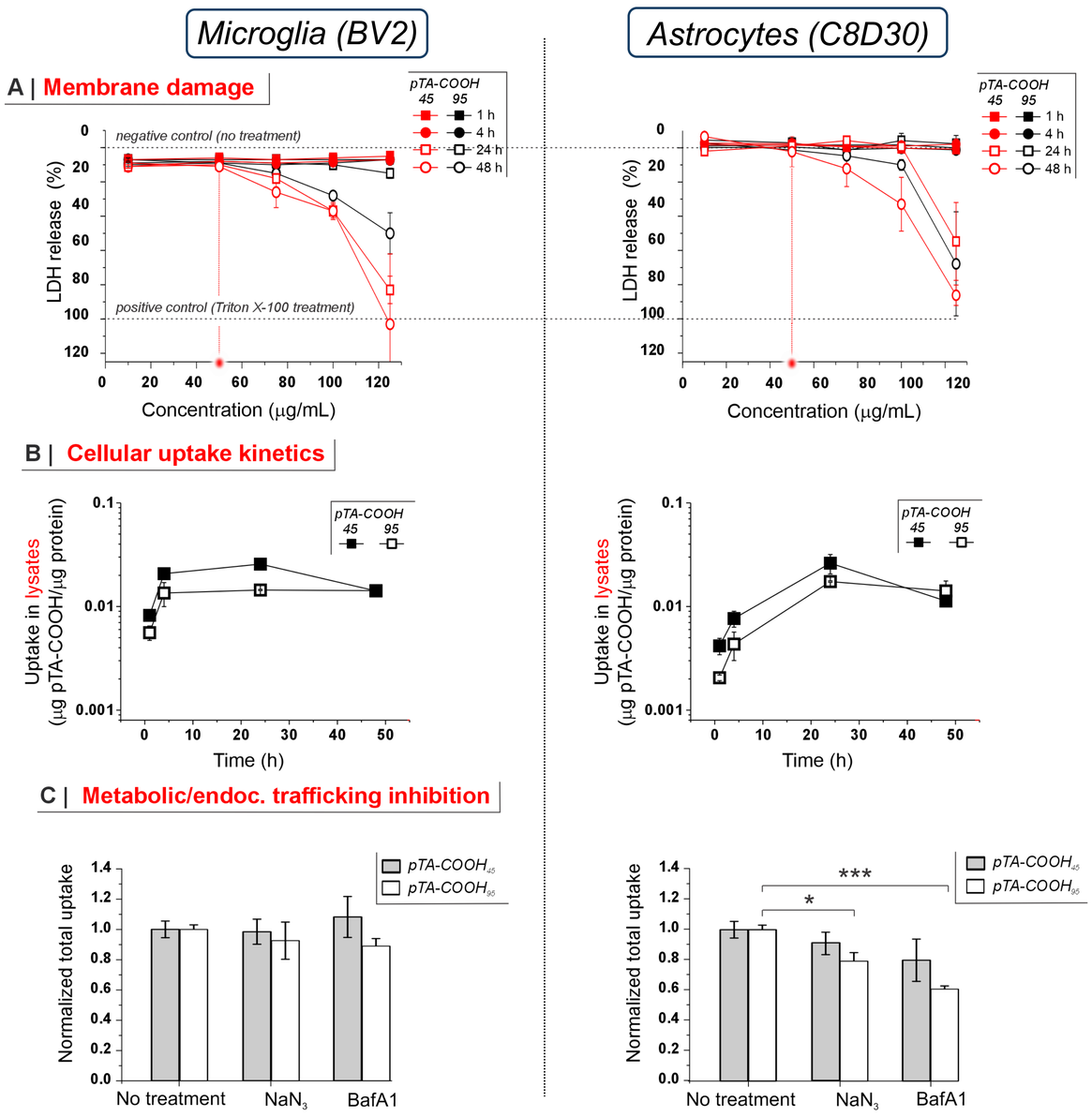


Droplet number scales with oxidation: reaction within a droplet accelerates before other droplets start reacting

In vitro assessment of PTA

Cytotoxicity and uptake

Two murine cell lines (BV2 microglia, C8D30 astrocytes) were exposed to PTA-$COOH_{45}$ (dispersible) and PTA-$COOH_{95}$ (soluble).



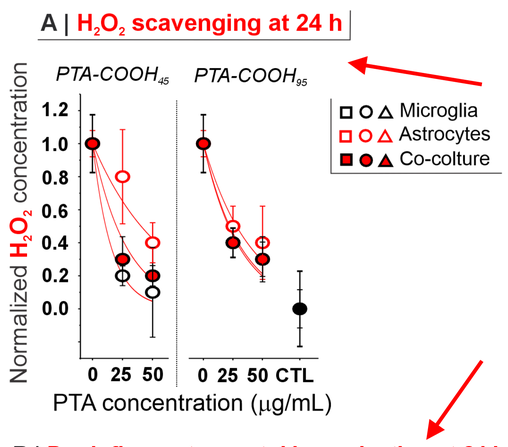
No decrease in viability with up to 50 (PTA-$COOH_{45}$) or 100 μg/mL (PTA-$COOH_{95}$) for up to 48 h.

Microglia: both polymers appear to undergo passive uptake.

Astrocytes: PTA-$COOH_{45}$ passive permeation; PTA-$COOH_{95}$ is, at least partially, endocyted.

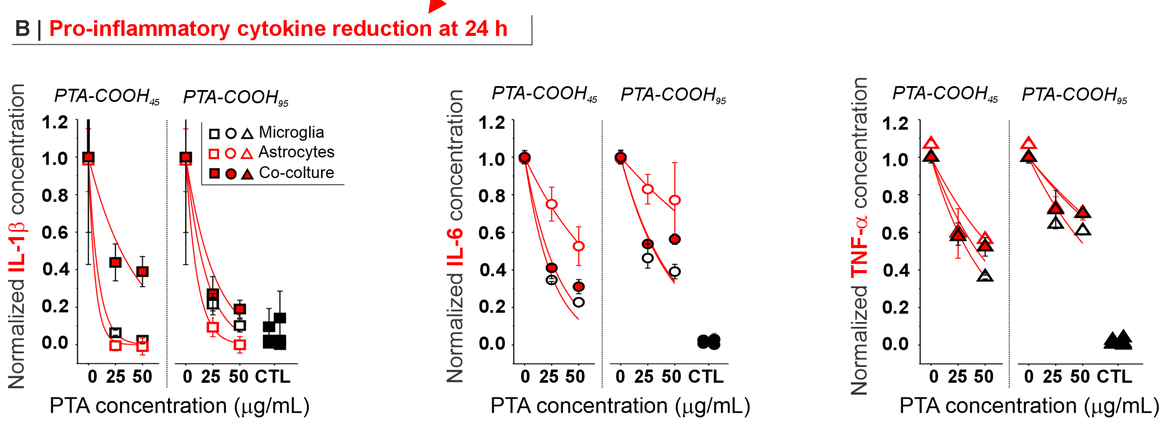
Anti-inflammatory potential

50 μg/mL PTA-COOH on LPS-activated BV2 and C8D30 cells.



PTA-$COOH_{45}$ was slightly more H_2O_2 scavenging than PTA-$COOH_{95}$ in the two cell lines (alone or co-culture).

PTA-$COOH_{45}$ reduced IL-1β, IL-6, and TNF-α. slightly more than PTA-$COOH_{95}$, possibly due to the higher uptake.



Conclusions

Poly(thioacetal)s scavenge ROS and have anti-inflammatory effects in **CNS-relevant cell models**, comparatively better than polysulfides.

This suggests their suitability as therapeutic agents for **oxidative stress-related pathologies**.

References

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