Oxidized Polysaccharides as Templates for Green Synthesis of Anti-inflammatory Polypyrrole Biomaterials

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INTRODUCTION: Polypyrrole (PPy) is a conductive polymer with significant potential in biomedicine due to its antioxidant and electrical properties. However, its broader application is hindered by poor processability, limited biodegradability, and the tendency of PPy to leach from composite matrices due to its lack of covalent bonding. Conventional methods to covalently anchor PPy often require toxic linkers, complex synthetic pathways, and provide minimal control over the PPy deposition. This work introduces a novel, green and versatile technology based on the spontaneous aldol condensation between pyrrole and dialdehyde polysaccharides (DAPs), demonstrated on two distinct biomaterial morphologies: electrospun nanofibers and injectable hydrogels, both exhibiting potent anti-inflammatory effects.

METHODS: The method is based on a spontaneous aldol condensation between the aldehyde groups of DAP and the pyrrole rings, covalently tethering pyrrole to the polysaccharide backbone, following its shape. This "pyrrole-decorated" template is bioactive on its own and can facilitate polymerization of added pyrrole, yielding a covalently bound DAP-PPy copolymer.

Nanofibers: Chitosan-based nanofibers were fabricated via electrospinning, utilizing DAC as a dual-function reagent that simultaneously crosslinks the chitosan via Schiff bases and anchors PPy (via aldol condensation).

Hydrogels: Injectable, shear-thinning hydrogels were formulated using soluble chitosan and DAC-anchored PPy, loaded with bone morphogenetic protein-2 (BMP-2) for bone defect regeneration.

RESULTS: The aldol condensation mechanism successfully anchored PPy to the polysaccharide matrices. The resulting covalently crosslinked chitosan/DAC/PPy nanofibers exhibited conductivities up to 11 mS/cm and enhanced mechanical and chemical stability. In vitro assays confirmed significant antibacterial activity against *S. aureus* and accelerated wound healing compared to neat chitosan nanofibers.

The composite hydrogels demonstrated excellent self-healing and shear-thinning properties, suitable for direct injection into the body. In a critical-size calvarial defect mouse model, the PPy-modified hydrogels effectively scavenged reactive oxygen species (ROS) and suppressed pro-inflammatory cytokines (IL-6), leading to reduced acute inflammation (lower CD45+ and CD68+ counts) and enhanced collagen deposition, higher early osteogenesis marker expression, and better bone regeneration.

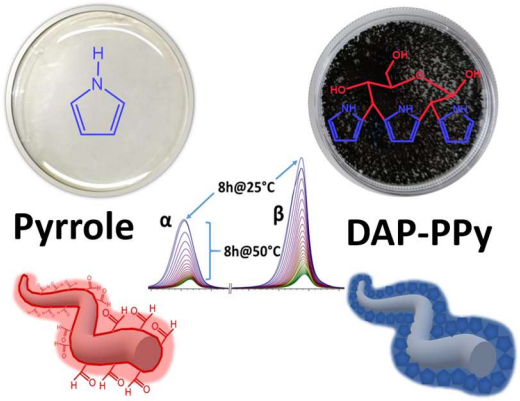

Fig. 1: Simplified scheme of the DAP-PPy reaction on the example of nanofibers.

DISCUSSION & CONCLUSIONS:
We have developed a green synthetic route to covalently bond PPy to polysaccharide matrices *via* aldol condensation. The resulting biomaterials combine the biocompatibility of polysaccharides with the conductivity and anti-inflammatory properties of PPy. Whether processed into nanofibers for wound dressings or hydrogels for bone regeneration, these composites provide a bioactive platform that modulates the immune response and accelerates tissue repair.

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REFERENCES: Vícha J, et al. ACS Sustain Chem Eng. 2025;13:8435-8446; Muchová M, et al. Int J Biol Macromol. 2025;308:142105.