

Chitosan derivatives as biomaterials: what the biomimetics lesson that we learn

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A Chinese proverb says: “Unintentionally planting willows yields unexpected shade”. Likewise, some research findings may come from no hypothesis.

Although our team started to fabricate chitosan 3D scaffolds for cartilage tissue engineering and peripheral nerve regeneration tubes since about 30 years ago, our deep interest for chitosan began in 2009 when I moved to the current university, where we started to use chitosan 2D membranes to grow mesenchymal stem cells and neural stem cells. While many types of stem cells can form spheroids on the membranes and it has become a convenient tool for us to determine whether the stemness of these cells is still present, the reason why stem cells can form spheroids on chitosan membranes remained a mystery after about a decade of investigation. In order to study central nervous system regeneration, our team started working on self-healing hydrogel, initially using a commercial soluble chitosan derivative, glycol chitosan (GC; Kodak), that soon became very expensive and pushed us to seek alternatives and synthesize various chitosan derivatives such as carboxyethyl chitosan (CEC), carboxymethyl chitosan (CMC), chitosan phenol (CP), chitosan catechol (CC), chitosan gallol, and chitosan boronic acid (CB), and to examine their structures by small-angle X-ray scattering. Our recent findings suggest that the side group modification of chitosan can strongly affect the mesoscale structure, producing nanoclusters, nanorods, or nanofibrils of chitosan in water medium. Some mesoscale structure may lead to multiscale self-assembly of chitosan under certain conditions. Meanwhile, linking other long-chain polymer with chitosan through various dynamic bonding can generate injectable hydrogel with hierarchical structure for tissue regeneration. Moreover, two different chitosan derivatives from side group modification can be combined through dynamic bonding to produce robust 3D-printable chitosan hydrogel under a low (2 wt%) solid content.

References: 2D membranes reviews: *Biotechnol. J.* 12: 1700064 (2017); *Appl. Sci.-Basel* 9: 627 (2019). GC, CEC, CMC: *Adv. Mater.* 27: 3518 (2015); *ACS Macro Lett.* 8: 1449 (2019); *ACS Appl. Mater. & Interf.* 14: 16023 (2022). CP: *Chem. Mater.* 33: 3945 (2021); *Adv. Funct. Mater.* 33: 2303853 (2023). CC: *Polymers* 16: 4614 (2022); *Int. J. Biol. Macromol.* 270: 132174 (2024). CB: *Carbohydrate Polymers* 363: 123737 (2025); *Carbohydrate Polymers* 381: 125140 (2026).