Smart drug delivery system based on nanocelluloses

Jing Xie and Jianshu Li

a) College of Polymer Science and Engineering, Sichuan University, Chengdu, 610065, China; b) State Key Laboratory of Polymer Materials Engineering, Sichuan University, Chengdu, 610065, China.
*Corresponding author: jianshu_li@scu.edu.cn

Keywords: Nanocelluloses; Drug delivery; Stimuli-sensitive

Nanocelluloses, also referred as nano-structured cellulose, including cellulose nanocrystals (CNC), cellulose nanofibrils (CNF) and bacterial cellulose (BC), are a family of abundant biomass and renewable materials in nature. Because of their excellent physical, mechanical, and biological properties, in particular biocompatibility, biodegradability, and low cytotoxicity, nanocelluloses have become indispensable for the design of new biomaterials. With decade’s development of cellulose factories, detailed preparations of nanocellulose are investigated. New types of cellulose derivatives like hydroxypropyl cellulose (HPC), carboxymethyl cellulose (CMC), hydroxyethyl cellulose (HEC) are synthesized to expand the use of the nanocellulose, as solvent for cellulose are usually either toxic or hard to remove. Chemical modifications, including sulfonation, esterification, etherification, silylation, amidation, etc., have been also widely used to functionalize nanocelluloses. For example, the thiolated hydroxypropyl cellulose possesses reversible thermal and redox sensitivities, which may have potential stimuli-responsive applications in the field of drug controlled release.

Performing excellent mechanical robustness, hydrophilicity, biocompatibility and good biodegradability, nanocelluloses have special functions, such as tissue repair, regeneration and healing, sensors, antimicrobial nanomaterials, shape memory materials and smart membranes, and so on. For instance, gold deposited on cellulose can be used for biomimetic sensor/actuator devices and micro-electro mechanical systems. Also, microfibril cellulose-based materials can modulate the release of H₂O₂ and O₂ for applications in wound sterilization and to accelerate wound healing. Among these applications, drug delivery draws tremendous attentions during past decades. Combining the advantage of nanocellulose and the ‘smart’ property of polymers by grafting techniques, like ‘graft from’ technique, ‘graft to’ technique and ring-opening polymerization, endow nanocellulose with controllability. Moreover, as smart polymers are flexible and can perform different conformations, like microparticle, membrane, capsule, hydrogel, etc., this strongly broadens the application field of nanocellulose system (Scheme 1).

Thermo-sensitive controlled-release microcapsule, which has a core layered with a water-soluble model drug particles and a thermo-sensitive shell composed of nano-sized thermo-sensitive hydrogels in ethy cellulose matrix. This thermo-sensitive shell behaves stimuli-responsive drug delivery property, which offers a composite system that can regulate their properties in the form of microcapsules. The hydrogel particles consisted of a newly synthesized composite latex with a poly(N-isopropylacrylamide) shell could reversibly change the shell thickness in water with response to an environmental temperature change. Membrane is also a widely used morphology in drug delivery system. Wu’s group designed a temperature and pH-responsive polymeric composite membranes. The composite membranes were prepared from nanoparticles of poly(N-isopropylacrylamide-co-methacrylic acid) dispersed in a matrix of a hydrophobic polymer, which could be used for controlled drug and protein delivery.

One kind of drug delivery system based on nanocellulose nanocrystal by in situ host-guest inclusion. β-cyclodextrin was first grafted on cellulose nanocrystal, then the pluronic polymer and α-cyclodextrin were attached by in situ inclusion, forming supramolecular hydrogels, as a drug carrier for doxorubicin. The doxorubicin can be released gradually in vitro, exhibiting the behavior of prolonged drug release. The mechanism behind the drug release in matrices has been elucidated by Ferrero, Massuelle and Doelker.

Nanocelluloses made from different raw materials can also show diverse drug delivery effects and mechanism. Laaksonen’s group compared drug release property in different nanofibrillar cellulose aerogels including microcrystalline cellulose, bacterial cellulose, quince seed and TEMPO-oxidized birch cellulose-based aerogels, showing sustained drug release except in microcrystalline cellulose. Cellulose nanowhiskers, cellulose microparticles, polycarbohydrate nanocellulose based aerogels and superabsorbent hydrogels are also developing as promising biodegradable carriers for drug delivery systems. These nanocellulose-based nanocomposite structures open up new possibilities as
Carriers for controlled drug delivery.

Combining stimuli-responsive materials, nanocelluloses and their derivatives (CNF, CMC, HPC, HEC, etc.) show great potential applications in drug delivery systems because of their outstanding biocompatibility, biodegradability and stimuli-responsiveness. Nanocellulose-based composites show great controlled drug delivery in diverse morphologies including microparticles, hydrogel, membrane and aerogel, and so on. With the present improvement and breakthrough of the nanocellulose modification techniques, nanocelluloses are drawing tremendous attentions in drug delivery systems and continue to grow in the future.

Scheme 1. Schematic illustration of the nanocellulose-based smart drug delivery systems. (Hydrogel image is reprinted with permission from ref 19. Copyright (2013) American Chemical Society)

ACKNOWLEDGMENTS

The authors are grateful for the financial support from the National Natural Science Foundation of China (Grant No. 21534008 and 51322303).

REFERENCES