SELF-ASSEMBLED LIGNOCELLULOSE MICELLES: A NEW GENERATION OF VALUE-ADDED FUNCTIONAL NANOSTRUCTURES

Xiaohui Wang [a] and Runcang Sun [a, b]

Lignocellulose-based self-assembled micelles have emerged as a new generation of value-added functional nanostructures that show promise to address issues concerning the depletion of non-renewable resources; also these materials may contribute to the growing enthusiasm of utilizing biomass resources. Lignocellulose micelles can be conveniently prepared by self-assembly of amphiphilic lignocellulose derivatives in aqueous solution. They show great potential for applications in disparate fields, e.g. drug delivery, bioimaging diagnosis, sensing, nanoreacting, and so on. However, as a new research topic, a lot of research work would be needed to find out the critical structural factors that correlate with the formation, stability, morphology, and flexibility of lignocellulose micelles.

Keywords: Lignocellulose micelles; Self-assembly; Drug delivery; Bioimaging

Contact information: a: State Key Laboratory of Pulp and Paper Engineering, South China University of Technology, Guangzhou, 510641, China; b: Institute of Biomass Chemistry and Technology, Beijing Forestry University, Beijing 100083, China, Mail to: fewangxh@scut.edu.cn; ynsun@scut.edu.cn

Emerging of Lignocellulose Micelles as Novel Functional Materials

Amphiphilic lignocellulose refers to those modified cellulose or hemicellulose macromolecules that contain both hydrophilic and hydrophobic segments. In an aqueous environment these molecules can aggregate into spherical, core-shell-like particles above their critical micelle concentrations (CMCs). The core is formed by the hydrophobic segments and is separated from the aqueous environment by the hydrophilic shell. As a result, micelles can be used to effectively solubilize, concentrate, and carry compounds that have poor solubility, low stability, or undesirable properties in the core structure. In comparison with other amiphiphilic surfactants, amphiphilic lignocellulose compounds are advantageous due to their good biocompatibility, biotolerability, biodegradability, and protein-rejecting properties. In addition, micelles using lignocellulose as raw materials are environmentally friendly, inexpensive to make, and available in large quantities. It could be expected that amphiphilic lignocellulose micelles would have tremendous potential and versatile applications in medicine, pharmacy, and sensing, etc.

Preparation of Amphiphilic Lignocellulose

Amphiphilic cellulose derivatives have been first prepared by hydrophobic modification of water-soluble cellulose derivatives, such as hydroxyethyl cellulose (HEC), carboxymethyl cellulose (CMC), hydroxypropyl cellulose (HPC), etc., with long-chain alkyl, acyl halides, or alkyl epoxy groups. Or in a reverse way, the amphiphilic

cellulose could be prepared by introducing hydrophobic groups to the cellulose backbone first, followed by the introduction of hydrophilic groups. Lately, more attention has been focused on preparing amphiphilic graft copolymers of cellulose, such as cellulose acetate phthalate, cellulose-g-poly(L-lactide), ethyl cellulose (EC)-g-polyacrylic acid (PAA), and HPC-g-poly(ε-caprolactone) by open-ring polymerization or atom transfer radical polymerization. The preparation of amphiphilic hemicellulose has not been specifically reported; however the modification methods for water- or alkaline- soluble polysaccharides could be easily adopted. It would be more meaningful if raw biomass residue such as bagasse or straw could be modified into a heteropolysaccharide amphiphile that has the ability of forming stable nanocapsules in the media of ionic liquid. By that way, the expense of making micelles would be minimized.

Potential Applications of Amphiphilic Lignocellulose Micelles

Drug delivery

The aim of drug delivery includes minimizing drug degradation and loss, preventing harmful side-effects, increasing drug bioavailability, and locating drug at a required zone in the body. Ideal drug delivery carriers should be made of biodegradable, biocompatible, and nontoxic materials and be at nanoscale range. Nanoparticles made of natural polysaccharides, such as chitosan, cellulose etc., would meet all the requirements. In comparison with solid nanoparticles, with which the drug can only be attached to the particle surface, core-shell structured polysaccharide nano-micelles are especially advantageous, owing to their ability to solubilize poorly soluble drugs with higher loading capacity and thus increase their bioavailability. Moreover, the hydrophilic shell protects the drugs in the core from hydrolysis and other biodegradation processes. Several studies have revealed that amphiphilic cellulose micelles exhibited no significant cytotoxic effect and represent a promising delivery vehicle for poorly soluble pharmaceuticals.

Bioimaging and diagnosis

Fluorescent or near-infrared (NIR) emissive micelle nanoparticles of block polymers have been obtained by loading conjugated fluorescent or NIR fluorophores into the core or shell of micelles. Once the particles' surfaces were modified with cell-permeable peptide, the micelles were able to reach dendritic cells intracellularly. And these micelles could be detected in vivo with fluorescent or NIR imaging at centimeter tissue depths with high sensitivity without disturbing cellular function. Although no study has been reported concerning the application of amphiphilic lingocellulose micelles in bioimaging, it is believable that a fluorescent compound (a NIR fluorophore) could also be loaded into amphiphilic cellulose micelles with high quality through similar treatment. And amphiphilic lignocellulose micelles would be more favorable as bio-imaging carriers due to their good biocompatibility and biodegradability.

Sensing, nanoreacting, and multitasking

Since amphiphlic lignocellulose could self-assemble into nanocapsules in aqueous solution, they may be environmentally friendly when used as nanosized reaction vessels for in-situ synthesizing functional nanoparticles like nano-Ag, quantum dots, nano-Fe_3O_4,

etc. And cost-efficient fluorescent sensors could also be developed by using lingo-cellulose aqueous micelles as a substrate for hydrophobic fluorophors. On the other hand, amphiphilic lignocellulose micelles have the potential to meet the requirements for multifunctionalization, e.g. targeting delivery, biobarrier avoidance, antifouling, and diagnostic imaging, because multiple functional materials could be coprecipitated into the core.

Challenges

Although so many exciting potential applications have been revealed for lignocellulose micelles, they cannot be successfully applied until their intrinsic short-comings have been carefully considered. For example, the formation and stability of micelles is concentration-dependent, which means they may dissociate upon dilution, especially in the case of those having higher CMC and non-rigid structure. This could be a serious problem for biological applications, including drug delivery and bio-imaging, because when delivered into body fluids, the surfactant concentration will be diluted by many orders of magnitude, possibly to below the CMC. Under these conditions, the micelles would disassociate, and the drug would pass between the micelle and the aqueous solution. The problem of instability can be avoided by preparing surfactant polymers with low CMC and rigid structure, which makes a strict requirement to the work of cellulose modification. Proper amphiphilic cellulose derivatives need to have a balanced hydrophobic domain and hydrophilic domain to make sure that stable micelles could be formed at very low concentration. Thus the modifying reaction must be precisely designed and controlled. On the other hand, the problem of instability of micelles could be overcome by cross-linking shell polymer or construction of an assembly that topologically resembles micelle architecture but with the surfactant chains covalently bound together. For those purposes, the polymers must contain reactive groups, or they need to be specifically modified to contain such groups.

Moreover, the substitution degree of hydrophobic and hydrophilic moieties, the ratio of hydrophobic to hydrophilic moieties, and the existence of salt ions, surfactants and biomacromolecules correlate well with the formation and stability of polymer micelles in aqueous solution. For the application of amphiphlic lignocellulose micelles, all of above correlations need to be investigated.