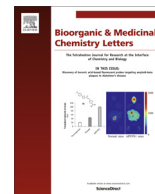




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Carbon nanodots as molecular scaffolds for development of antimicrobial agents



Maria Ngu-Schwemlein^{a,*}, Suk Fun Chin^b, Ryan Hileman^a, Chris Drozdowski^a, Clint Upchurch^a, April Hargrove^a

^a Department of Chemistry, Winston-Salem State University, Winston-Salem, NC 27110, USA

^b Department of Chemistry, Universiti Malaysia Sarawak, 94300 Kota Samarahan, Sarawak, Malaysia

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ABSTRACT

We report the potential of carbon nanodots (CNDs) as a molecular scaffold for enhancing the antimicrobial activities of small dendritic poly(amidoamines) (PAMAM). Carbon nanodots prepared from sago starch are readily functionalized with PAMAM by using *N*-ethyl-*N'*-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC) and *N*-hydroxysuccinimide (NHS). Electron microscopy images of these polyaminated CNDs show that they are approximately 30–60 nm in diameter. Infrared and fluorescence spectroscopy analyses of the water-soluble material established the presence of the polyamidoaminated moiety and the intrinsic fluorescence of the nanodots. The polyaminated nanodots (**CND-PAM1** and **CND-PAM2**) exhibit in vitro antimicrobial properties, not only to non-multidrug resistant bacteria but also to the corresponding Gram-negative multidrug bacteria. Their minimum inhibitory concentration (MIC) ranges from 8 to 64 µg/mL, which is much lower than that of PAMAM G1 or the non-active PAMAM G0 and CNDs. Additionally, they show synergistic effect in combination with tetracycline or colistin. These preliminary results imply that CNDs can serve as a promising scaffold for facilitating the rational design of antimicrobial materials for combating the ever-increasing threat of antibiotic resistance. Moreover, their fluorescence could be pertinent to unraveling their mode of action for imaging or diagnostic applications.

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The ever-increasing incidence of bacterial resistance to existing antibiotics has created a need to broaden the targets as well as to develop new antimicrobials and strategies to combat antibiotic resistant bacteria.^{1,2} Carbon nanodots (CNDs) are a fascinating new class of nanomaterials that are promising molecular templates for various different types of applications including imaging, sensing, drug delivery, photocatalysis, and more.^{3–6} They are readily prepared from starch and other carbonaceous sources^{7–9} and their low toxicity index promises numerous biomedical applications besides their fluorescent properties.^{10,11}

Carbon nanodots, like their nanotube congeners, offer reactive surface functional groups that can be oxidized by acid reflux to generate carboxylic acid containing dots.^{8,12–14} Such surface decorated functional moieties on the carbon dots allowed for further passivation, with various compounds such as *N*-acetyl-cysteine, PEG₁₅₀₀N, and other polymers, to improve their fluorescence properties.^{15–17} Accordingly, CNDs could serve as a molecular scaffold

for grafting small polycationic amines. The nanoscale carbon dots offer high surface areas suited for concentrating such cationic densities for enhanced antimicrobial activity. Structurally large polycationic compounds including poly-lysines, cationic amphipathic peptides, and large polyamine dendrimers have been reported to exert antimicrobial activities. They disrupt the integrity of bacterial membranes, which possess an overall net anionic charge, via favorable electrostatic and hydrophobic interactions.^{18–20} Moreover, some of these polycationic compounds enhanced the uptake of small hydrophobic antibiotics into the bacterium, and consequently, presented synergistic effects. For example, an alpha-helical cationic peptide was reported to exert a potent synergistic effect with chloramphenicol against some types of bacteria.²¹

Poly(amidoamines) (PAMAM) dendrimers consist of an interior ethylene diamine core surrounded by successive branching layers (generations) that terminate with amino groups.^{20,22} Although the higher generation PAMAM dendrimers (greater than generation three, G3) exhibit antibacterial properties, the flexible and open lower generation dendrimers lacks significant efficacy.²⁰ Therefore, we explore carbon nanodots as a molecular scaffold

* Corresponding author. Tel.: +1 336 750 2919; fax: +1 336 750 2549.

E-mail address: Schwemleinmn@wssu.edu (M. Ngu-Schwemlein).