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Halloysite nanotube with silver and tannic acid: A sustainable Nano-enabled antibacterial combination therapy (NeACT) for application in animal agriculture

Satwik Majumder[a], Charles Viau, Amarpreet Brar, Jianguo Xia, Saji George

[a]Department of Food Science and Agricultural Chemistry, Macdonald Campus, McGill University, 21,111 Lakeshore Ste Anne de Bellevue, Quebec H9X 3V9, Canada

The prevalence of antimicrobial resistance (AMR) among pathogenic bacteria warrants alternate therapeutic strategies that are efficient in remediating zoonotic infections. Combination therapy with more than one antimicrobial with complementary action has shown possibilities to prevent or slow down AMR. The application of nanoclay-based biomaterials could, however, resolve challenges of poor bioavailability, cytotoxicity, stability, release, and overdosing and play a significant role in formulating cost-effective sustainable therapeutics. In this study, a nanocomposite (GH-TA-Ag-NT) containing nanosilver (AgNPs) grafted onto tannic acid (TA)-modified halloysite nanotubes (HNT) was generated and tested for physicochemical and antibacterial properties. The Transmission Electron Microscopy, Fourier Transformed Infra-Red, Dynamic Light Scattering, and X-ray Diffraction Spectroscopies confirmed the synthesis of the nanocomposite. GH-TA-Ag-NT demonstrated enhanced stability, drug-bioavailability with a slow-release of Ag+ and TA. The nanocomposite showed excellent antibacterial performance in comparison to commercial TA-stabilized AgNPs when tested against E. coli ATCC 25922, S. aureus ATCC 25923, and a multi-drug resistant (MDR) *Salmonella enterica* serovar Typhimurium (isolated from infected swine) owing to the combinatorial effect mediated through anti-efflux/anti-biofilm properties, oxidative stress, loss of bacterial membrane potential, and integrity. The toxicity and antibacterial efficiency of GH-TA-Ag-NT to remediate gastrointestinal infection were demonstrated in the S. Typhimurium infected *Caenorhabditis elegans* model. The nanocomposite was less toxic, reduced Salmonella colonization significantly in 24 h of exposure, and improved worm survivability. In summary, we demonstrated a unique and novel strategy to counter AMR bacteria applying Nano-enabled Antibacterial Combination Therapy (NeACT) with GH-TA-Ag-NT with multi-functional characteristics that could resolve the common challenges of poor bioavailability, cytotoxicity, stability, drug release, and overdosing. Thus, it warrants potential use as a therapeutic against zoonotic pathogens in animal agriculture.

Keywords: Animal agriculture, Sustainable nanotechnology, Halloysite nanoclay, Tannic acid, Nanosilver, Nano-enabled Antibacterial Combination Therapy (NeACT), Antimicrobial resistance (AMR), Zoonotic infections, *Salmonella enterica* serovar Typhimurium, Caenorhabditis elegans.

Biography:

My research addresses the implications and application of sustainable nanotechnology in the field of food and agricultural safety and security. The extensive use of antibiotics relevant to human health in animals has contributed significantly to the emergence and transmission of antimicrobial resistance (AMR) through direct contact from infected animals or the food supply chain. Continuous surveillance for AMR among bacterial isolates from farms is vital for the effective management of zoonotic infections. Therefore, I am monitoring antimicrobial resistance and virulence characteristics in bacterial isolates from infected livestock of Canadian farms through phenotypic and genotypic studies. Combination therapy with more than one antimicrobial agent comprised of complementary mechanisms of action has shown possibilities to prevent or slow down AMR. However, such therapies have still shown vulnerability towards AMR or faced challenges of poor bioavailability, cytotoxicity, stability, release, and overdosing. The application of nanomaterials could resolve these issues and play a significant role in advanced formulations of cost-effective and sustainable therapeutic strategies as a multiple drug carrier. Hence, the ultimate goal of my research is to create nano-enabled therapeutics to restrict bacterial pathogenicity and thus, zoonotic infections.