Assessment of Silver Carboxylate's Cytotoxicity in Primary Cell Lines: an Early Characterization of its Safety Profile Relating to Wound Care.

2022 Lifespan Research Day Abstract

Research Category: Clinical & Translational, Basic Science, Innovation

Primary Research Location: Diane Weiss Center for Orthopaedic Trauma Research, Rhode Island Hospital, RI, USA

Funded By: Research reported in this presentation was supported by the Rhode Island Institutional Development Award (IDeA) Network of Biomedical Research Excellence from the National Institute of General Medical Sciences of the National Institutes of Health under grant number P20GM103430 and P20GM121344. This research was also supported by NIAIG grant R03AI159776 and in part by NIH/NIAID R25.

Authors(s):

Benjamin Stone, Medical Student, Brown University. Dept of Orthopedics
Colin Whitaker, Medical Student, Brown University. Dept of Orthopedics
Olive Cooper, Undergraduate Student, Tougaloo College. Dept of Orthopedics
Drew Clippert, Undergraduate Student, Rhode Island Hospital, Brown University. Dept of Orthopedics
James Hong, Undergraduate Student, Brown University. Dept of Orthopedics
Neel Vishwanath, Medical Student, Rhode Island Hospital, Brown University. Dept of Orthopedics
Valentin Antoci, MD, PhD, Associate Professor, Rhode Island Hospital, Brown University. Dept of Orthopedics
Christopher Born, MD, Professor, Rhode Island Hospital, Brown University. Dept of Orthopedics
Dioscaris Garcia, PhD, Assistant Professor, Rhode Island Hospital, Brown University. Dept of Orthopedics

Abstract

Background & Aim: The rise of multi−drug resistant bacteria, has prompted a dire need for the development of antibiotic−independent antimicrobial agents. The Diane N. Weiss Lab for Orthopaedic Trauma Research has developed a novel formulation composed of silver carboxylate suspended in a 95% titanium dioxide (TiO2)/polydimethyl siloxane (PDMS) matrix. To characterize safety in human tissues, we performed the MTT cell viability assay for osteoblasts (OBs), keratinocytes (KTs), and skeletal muscle cells (SkMCs) and compared the cytotoxicity profile to that of cruder forms of silver as well as last resort antibiotics commonly used to treat surgical infections.

Methods: Human osteoblasts, keratinocytes, and skeletal muscle cells were cultured at 1x104 CFU/ml. The Promega CellTiter 96 Non−Radioactive Cell Proliferation Assay protocol was followed to perform MTT after adding the following conditions: 1X silver carboxylate, 10X silver carboxylate, vancomycin (5ug/ml, 50ug/ml), linezolid (2µg/ml, 20µg/ml), tobramycin (5µg/ml, 50µg/ml), polymyxin E (2µg/ml), crude silver nanoparticles (10nM, 30nM), and colloidal silver (100nM, 300nM). The negative controls (cell blank and 95% TiO2/PDMS matrix−only) and positive controls (1% triton X and 100% silver carboxylate with no matrix) were also utilized.

Results: OBs notable cell viabilities compared to the cell blank: 1X silver carboxylate (61.8%) had comparable or less cytotoxicity compared to vancomycin (50ug/ml) (67.7%), tobramycin (50µg/ml) (12.5%), and silver nanoparticles (30nM) (55.6%). KTs notable cell viabilities compared to the cell blank: 1X silver carboxylate (38.7%) had comparable or less cytotoxicity compared to linezolid (20µg/ml) (2.5%), tobramycin (50µg/ml) (41.5%), silver nanoparticles (10nM) (47.8%), silver nanoparticles (30nM) (31.9%), and colloidal colloidal silver (300nM) (38.0%). SkMCs notable cell viabilities compared to the cell blank: 1X silver carboxylate (92.9%) had comparable or less cytotoxicity compared to vancomycin (50ug/ml) (80.4%), linezolid (2µg/ml) (22.8%), linezolid (20µg/ml) (0.8%), tobramycin (5µg/ml) (82.0%), tobramycin (50µg/ml) (57.1%), polymyxin E (2µg/ml) (0.7%), silver nanoparticles (10nM) (97.3%), silver nanoparticles (30nM) (63.5%), colloidal silver (100nM) (86.1%), and colloidal silver (300nM) (89.3%).

Conclusion: We observed comparable or lower cytotoxicity for 1X silver carboxylate compared to crude silver formulations and concentrations of commonly used last resort antibiotics, particularly in the SkMC.

Clinical Implications: Although these data are preliminary, this promising safety profile aids in supporting the use of silver carboxylate in vivo.