Assessment of the Safety and Application of Silver Carboxylate as a Pre-Surgical Dressing
Geronimo Garcia¹, Patrick Barhouse¹, Drew Clipper³, Benjamin Stone¹, Colin Whitaker¹, Christopher T Born MD¹, Valentin Antoci MD PhD²,³, Dioscaris R Garcia PhD³
¹Brown University, Warren Alpert Medical School, Providence, RI, ²University Orthopedics, East Providence, RI
Presenting Author: Geronimo Garcia, geronimo_garcia@brown.edu

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INTRODUCTION
The incidence of surgical site infections (SSIs) in the United States is linked to 300k-500k cases annually and imposes monetary costs exceeding $1.5 billion to our healthcare system.¹ The accelerating rise of antimicrobial resistance necessitates innovative approaches to combat this increasingly challenging problem. A significant challenge in preventing SSIs is the limited efficacy of current pre-surgical sterilants.² Silver carboxylate (AgCar) is a novel organometallic antimicrobial compound which achieves predictable pharmacokinetics of loading and release via a TiO₂/polydimethylsiloxane (TiO₂/PDMS) matrix. Previous studies have provided evidence of AgCar’s efficacy against drug-resistant pathogens in prosthetic liners, sutures, spinal implants and as a pre-surgical skin preparation in combination with chlorhexidine gluconate (CHG) prep.³ The unique attributes of AgCar chemistry, including penetration into the pilosebaceous pores, controlled release, and broad-spectrum antimicrobial efficacy, position it as a noteworthy option for infection prophylaxis. AgCar has also demonstrated comparable antimicrobial efficacy to last-resort antibiotics against bacteria commonly encountered in SSIs. This study explores AgCar’s cytotoxic profile on human-derived primary endothelial cells (ECs) and keratinocytes in the context of superficial wound healing, and its potential application as an alternative antimicrobial pre-surgical dressing.

METHODS
MTT Assay
After 24 hours, primary cell lines involved in wound healing were exposed to conditions of 1x silver carboxylate, 10x silver carboxylate, vancomycin (5µg/ml), tobramycin (5µg/ml), tobramycin (50µg/ml), linezolid (2µg/ml), linezolid (20µg/ml), and polymyxin E (2µg/ml). 10µM silver nanoparticles, 30nM silver nanoparticles, 100nM colloidal silver, and 300nM colloidal silver, cell blank and a 95% TiO₂/PDMS matrix only conditions were used as negative controls and 100% silver carboxylate and 1% Triton X were used as positive controls. Silver carboxylate conditions, TiO₂/PDMS matrix only, and 100% silver carboxylate positive control were added by dip coating 2 mm inert glass beads. After 24 hours, cell viability was measured by Promega Cell Titer 96 Non-Radioactive Cell Proliferation Assay protocol (MTT assay) and spectrophotometry at a wavelength of 570 nm. Optical density of each condition was then compared to optical density of the cell blank to determine percent cell viability. Replicates of n=15 were performed for each condition. The MTT assay was performed for each condition. Statistical analysis was completed using Excel for T-Tests with statistical significance (p < 0.05).

RESULTS
Silver carboxylate at 10x MIC demonstrated significant cytotoxicity across all cell lines per the MTT assay. 1x MIC silver carboxylate demonstrated comparable or lower cytotoxicity than conventional silver formulations and certain concentrations of last-resort antibiotics. Cytotoxicity at 10x silver carboxylate concentrations approximated that of positive controls. Several higher antibiotic concentrations commonly employed in wound care exhibited cytotoxicity comparable to positive controls. ECs treated with 1X Silver Carboxylate showed higher viability compared to all tested antibiotics and crude silver conditions. Per Resazurin assay, 1x MIC silver carboxylate exhibited statistically insignificant impact on cell viability for endothelial cells, whereas concentrations of 10x to 150x resulted in statistically significant decreased cell viability in ETs and keratinocytes (p < 0.001).

DISCUSSION
Ongoing research is investigating the molecular mechanisms of AgCar as well as exploring methodologies to decrease cytotoxicity beyond the 1x MIC. Overall, our research underscores the potential for silver carboxylate in pre- and post-operative surgical wound healing, particularly when combined with current preparations. Further research will reveal its antimicrobial potential, especially in surgical skin preparation and wound care synergy, offering promise as an additional tool for preventing surgical site infections.

CLINICAL RELEVANCE
Silver carboxylate embedded within the TiO₂-PDMS matrix holds promise as a versatile antimicrobial option for orthopedic surgical sites. Its potential use as a stand-alone or synergistic pre-operative sterilant could overcome antibiotic limitations and antibiotic resistance. The concept of enhanced combined efficacy presents intriguing possibilities in augmenting the capabilities of currently utilized antimicrobial therapies.

REFERENCES

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