Phytochemicals for Periprosthetic Joint Infection Prophylaxis against *Staphylococcus aureus*

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Introduction. Infection, especially from *Staphylococcus aureus (s. aureus),* is a leading cause of total joint arthroplasty failure. Surgeons often incorporate prophylactic antibiotics into orthopedic biomaterials, such as calcium phosphate spacers or acrylic bone cement. However, antibiotic resistance necessitates alternative antibiotics. This project evaluates antimicrobial efficacy of three phytochemicals – thymoquinone, magnolol, and usnic acid – against *S. aureus.*

Methods. We evaluated each compound's solubility in multiple solvents. In accordance with the Beer-Lambert law, absorbance and concentration are linearly related within the solubility limit. To identify the minimum inhibitory concentration (MIC) that prevents bacterial growth, we exposed *S. aureus* inoculums to dilutions of each phytochemical. We performed MIC assays in triplicate for each combination of phytochemical, solvent, and bacterial strain.

Results. Thymoquinone's solubility in phosphate buffered saline (177 µg/mL) is approximately one-third of its solubility in acetone (500 µg/mL). Similarly, the other phytochemicals are more soluble in hydrophobic solvents. Usnic acid is potent against *S. aureus* with an MIC of 3 µg/mL. Both magnolol (MIC = 8 µg/mL) and thymoquinone (MIC = 8 µg/mL) are effective against methicillin-resistant *S. aureus* strains. Thymoquinone has the most robust activity, with activity in multiple solvents against four *S. aureus* strains.

Conclusions. Magnolol, thymoquinone, and usnic acid are similarly efficacious as conventional antibiotics are against *S. aureus.* We are currently investigating potential synergism between these phytochemicals and conventional antibiotics. Synergistic pairings could further stave off antibiotic resistance. Future studies will investigate whether the relatively low solubility of these compounds prolongs the timeframe of elution from orthopedic biomaterials.

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