**Influence of Trehalose Coating on the Bioactivity and Structural Properties of Bioglass 45S5 and Gallium-Doped Bioglass 45S5 for the delivery of antimicrobials: An In Vitro Characterization Study**

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**Background:** Bioglass 45S5, renowned for its bioactivity and ability to bond with bone tissue, is integral to tissue engineering. Its composition fosters hydroxyapatite layer formation, crucial for bone integration. Recent advancements include gallium-doped Bioglass 45S5, enhancing antimicrobial properties and bone formation. Trehalose coatings are explored to stabilize and improve bioactivity. This study examines the influence of trehalose coatings on the bioactivity and structural properties of Bioglass 45S5 and its gallium-doped variant for antimicrobial delivery, employing various in vitro characterization techniques to evaluate their efficacy and potential in biomedical applications.

**Methods:** Bioglass core 45s5 and 45s5Ga doped was coated with disaccharide at ratios of 1:1, 1:2, and 1:3. The resulting mixture was stirred, centrifuged, and washed with PBS buffer. The coated particles were collected, lyophilized, and loaded with 0.5% w/v, 1% w/v and 1.5% w/v of antibiotic solution. The particles were then analyzed for loading efficiency, size distribution, and zeta potential. In vitro drug release was carried out using a dialysis tubing method for 168 hours, and the samples were analyzed on LC20AT HPLC using C18 column at 280 nm on SPD-M20A-prominence diode array detector. Antimicrobial characteristics were analyzed using the zone of inhibition assays and the pH of blank and loaded particles were tested in SBF for 7, 14 and 21 days. Invitro dissolution testing of Bioglass 45s5 and 45s5Ga doped coated with disaccharide were carried out in simulated body fluid (SBF) to identify the hydroxyapatite forming behavior of Bioglass and calcium release was analyzed using atomic absorption spectroscopy (AAS). The obtained results were analyzed using GraphPad PRISM.

**Results:** The size distribution of particles in formulations F2l (BG45s5-T-T) and F4l (BG3%Ga-T-T) increased with higher antibiotic loading concentrations. For F2l, D (10) was 7.11 ± 0.806 µm, D(50) was 26.4 ± 1.730 µm, and D(90) was 53.7 ± 7.95 µm. For F4l, corresponding values were 4.61 ± 0.279 µm, 17.7 ± 0.425 µm, and 36.1 ± 1.32 µm, respectively. The zeta potential of antibiotic-loaded formulations decreased significantly compared to blank formulations ($p<0.0001$). FTIR analysis revealed siloxane and phosphate peaks, while Raman microscopy provided detailed molecular characterization. SEM images showed irregularly shaped particles with rough surfaces, indicative of a broad size distribution and high surface area. The Raman spectra indicated significant peaks around 1000-1500 $cm^{-1}$, corresponding to phosphate groups, with changes over time suggesting hydroxyapatite formation. The AAS analysis showed a continuous release of Ca+ for a period of 21 days when the bioglasses were treated in SBF. The cumulative drug release from formulations F2l-BG45s5-T-T-1.5% and F4l-BG3%Ga-T-T-1.5% closely followed the Korsmeyer-Peppas model ($R2 = 0.92$), showing an increase in percentage release with higher drug loading ($p<0.05$).

**Conclusions:** The study demonstrated that trehalose coating enhances the bioactivity and structural properties of Bioglass 45S5 and gallium-doped Bioglass 45S5, facilitating controlled antimicrobial delivery.