

# MICROFLUIDIC FABRICATION OF ALGINATE MICRODROPLETS FOR PHOTODYNAMIC ANTIMICROBIAL THERAPY

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Antimicrobial resistance has become a critical global health issue in 21<sup>st</sup> century, as bacterial tolerance to all currently used antibiotics has been detected and only a few novel medications are being developed [1]. In these circumstances antimicrobial photodynamic therapy (aPDT) has emerged as a promising alternative for the treatment of chronic wound infections. This method uses light-activated photosensitizers to generate reactive oxygen species (ROS) that kill pathogens without causing resistance. Methylene blue (MB) stands out among photoactive molecules because of its established clinical use, broad antimicrobial efficacy, and efficient absorption of red light (660–670 nm), which allows deeper tissue penetration [2].

To localize methylene blue exposure and support wound healing, the photosensitizer is commonly immobilized within alginate-based hydrogel systems. Alginate provides a biocompatible and optically transparent matrix that helps confine photodynamic activity and reduce off-target effects. However, most existing approaches rely on bulk hydrogels or polydisperse beads produced by batch emulsification, which result in broad size distributions and poorly controlled methylene blue loading. Therefore, photodynamic dosing remains undefined and difficult to reproduce. Moreover, despite the central role of ROS in aPDT, few researchers have quantified its output on a per-bead basis or evaluated how ROS generation evolves over repeated light activation cycles. These limitations restrict the predictability, optimization, and long-term applicability of alginate-based aPDT systems.

To address these challenges, a water-in-oil droplet microfluidic approach was developed for the fabrication of alginate microbeads. Highly monodisperse droplets were generated using a polydimethylsiloxane (PDMS) on glass microfluidic chip featuring a cross-junction geometry. Droplet formation and gelation were optimized by tuning aqueous and oil phase flow rates, alginate concentration, Tween 80 surfactant content in mineral oil, and calcium chloride crosslinking conditions. The resulting microbeads were characterized by optical microscopy to assess size, uniformity, and structural stability. Following methylene blue loading, reactive oxygen species generation was quantified on a per bead basis under controlled light activation, enabling direct evaluation of photodynamic behavior across microbead populations.

In summary, this work establishes a quantitative and reproducible framework for controlled antimicrobial photodynamic therapy dosing, enabling association between microbead design parameters and photodynamic output. Such an approach may facilitate the development of localized, reusable antimicrobial platforms, including wound dressings, catheter or implant coatings, and flow-based disinfection systems requiring precise photodynamic control.

**Keywords:** Microfluidics, Photodynamic Antimicrobial Therapy, Antimicrobial Resistance

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[1] E. M. Darby et al., "Molecular mechanisms of antibiotic resistance revisited," *Nat. Rev. Microbiol.*, vol. 21, no. 5, pp. 280–295, May 2023, doi: 10.1038/s41579-022-00820-y.

[2] A. Solovieva et al., "Methylene Blue Solid Alginate Gels for Photodynamic Therapy: The Peculiarities of Production and Controlled Release of the Dye," *Polymers*, vol. 16, no. 19, p. 2819, Jan. 2024, doi: 10.3390/polym16192819.