



INSTITUTIONEN FÖR KEMI OCH MOLEKYLÄRBIOLOGI

Biophotonics Targeting Pharmaceutical Challenges **Focusing on photopharmaceutical and antimicrobial delivery studies**

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Abstract

The study of the interaction between light and biological matter, called *biophotonics*, contributes to our understanding of biological systems - from subcellular compartments up to the human organ system. Herein, light is employed as a tool to understand delivery of novel photopharmaceutical and antimicrobial systems to bacteria, cells, and tissue.

The first part of this thesis (papers I and II) focuses on production of toxic species via photoactivation of a compound, both in cells and tissue, using two photon excitation (2PE). 2PE studies using near infrared excitation (NIR) afford deeper light penetrations depths in tissue. Novel methods for fluorescence reporting were developed to monitor penetration and localization of compounds, and *via* spectral signal from Förster resonance energy transfer (FRET) to monitor release in real-time.

Nanoparticles are becoming increasingly interesting as drug delivery systems. Multiphoton microscopy (MPM) and spectral analysis were used to evaluate particles for potential dermal drug delivery in paper III. Inherently luminescent silica particles revealed the size-dependent penetration of the particles in skin by combining *ex vivo* diffusion studies with 3D imaging and 2PE spectral detection and analysis.

The final part of this thesis (papers IV – VII) combines photoactivation with drug delivery systems to focus on the study and potential treatment of bacterial infections. Charge-functionalization of cyclodextrins (CDs) for optimal delivery to biofilms was evaluated. It was found that positively charged CDs better distribute in a *Staphylococcus epidermidis* biofilm environment. Eliminating biofilm cultures without the use of antibiotics is explored by applying phototherapy with NIR 2PE. It was demonstrated that curcumin, the active ingredient in turmeric, can be targeted to kill bacteria within 3D regions as small as 1 x 1 x 1 μm .

Taken together, this work developed biophotonics approaches for studying delivery of photopharmaceuticals and antimicrobials to biological systems through application of MPM, spectral imaging, photoactivation, and development of model systems.

Keywords: Multiphoton microscopy, two photon excitation, super resolution microscopy, fluorescence imaging, drug delivery, nanoparticles, cyclodextrins, antibiotics, microbial biofilms, *Staphylococcus*, photodynamic inactivation