

TIME AND REGIOSELECTIVE DRUG RELEASE BY TWO-PHOTON ABSORPTION FOR APPLICATION IN EYE DISEASE THERAPY

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INTRODUCTION: Cataract is world-wide one of the most widespread eye diseases. Its treatment is carried out by operative removal of the opaque human lens followed by implantation of a polymeric intraocular lens implant. In Germany approximately 400,000 intraocular lenses are implanted every year. Post capsule opacification (secondary cataract) is the major complication leading to reopacification due to the proliferation of lens epithelial cells at the implants surface. It is not desirable to add cell toxic drugs at the time of the implantation because wound healing is negatively affected. The goal of our research is the development of reservoirs for the postoperative, noninvasive medical treatment of post capsule opacification based on drug-loaded methacrylate-type polymers [1,3].

Controlled drug release is accomplished by photo-triggered cleavage of the covalently bound drug from the polymer. In this context we have investigated $[2\pi+2\pi]$ cycloreversion reactions of cyclobutane-type photodimers which act as a photolabile linker between drug and polymer [2]. The photochemically induced cleavage is performed by two-photon absorption processes with help of 532 nm pulses of a conventional frequency-doubled Nd:YAG laser system.

Two-photon organic photocleavage reactions offer several advantages over their customary single-photon induced analogues. Using pairs of VIS photons rather than single UV photons confines the release to areas which cannot be directly optically addressed due to cover layers, i.e. the cornea, which have a high absorption at the single-photon absorption wavelength (Fig. 1). Moreover two-photon absorption processes are dependent on a spatial and temporal overlap of the incident photons. Therefore precise three-dimensional spatial as well as temporal control of the drug release can be achieved noninvasively.

Fig. 1: Photochemically triggered drug release from a polymeric intraocular lens. (A) UV light is strongly absorbed by the cornea. (B) Two-photon absorption (TPA) of photons of the visible allows to induce drug release because in the visible the cornea has very low absorption.

RESULTS & CONCLUSIONS: The synthesis of the polymeric lens material was accomplished in only two steps. First, a methacrylate based copolymer modified with drug linking sites was prepared. In a second step drug molecules were photochemically loaded onto the copolymer.

Drug release from the copolymer was performed photochemically via single-photon excitation with UV light and via two-photon excitation with laser light of the visible. In both cases the photochemical deliberation of the drug from the copolymer was investigated by UV/VIS spectroscopy and HPLC analysis. Drug diffusion out of copolymer films was monitored after photochemical release.

REFERENCES: ¹N. Hampp, H-C. Kim, S. Kreiling, L. Hesse, A. Greiner, *Proc. SPIE*, in press. ²H-C. Kim, S. Kreiling, A. Greiner, N. Hampp, *Chem. Phys. Lett.* (2003) **372**:899. ³N. Hampp, L. Hesse, A. Greiner, W. Heitz, DE 199 55 836 C 1

