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Hollow resorbable fiber for combined light and drug delivery: fiber development and analysis of release kinetics / Milanese, Daniel; Barolo, Claudia; Visentin, Sonja; Boetti, Nadia; Barbero, Nadia; Pugliese, Diego; Janner, Davide; Bertiond, Cecilia; Ginistrelli, Edoardo. - ELETTRONICO. - 10413:(2017), pp. 1-3. (Intervento presentato al convegno European Conference on Biomedical Optics 2017 (ECBO 2017) tenutosi a Munich nel 25-29 Giugno 2017) [10.1117/12.2284313].

Availability:

This version is available at: 11583/2749087 since: 2019-08-30T16:46:55Z

Publisher:

SPIE-INT SOC OPTICAL ENGINEERING

Published

DOI:10.1117/12.2284313

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Hollow resorbable fiber for combined light and drug delivery: fiber development and analysis of release kinetics

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Abstract:

A hollow bioresorbable phosphate glass fiber was developed and used for drug and light delivery. The interaction between organic molecules and the fiber's internal surface was studied. Promising results for the release of Rose Bengal were obtained.

OCIS codes: (160.1435) Biomaterials; (160.2290) Fiber materials; (70.5180) Photodynamic therapy.

1. Introduction

Photodynamic Therapy (PDT) has been widely studied in the past decade as an effective method to treat malignancies. Initially, this procedure involves the binding of a selective photosensitizer to cancer cells. Subsequently, excitation with appropriate light source activates the photochemical agent, resulting in cancerous cells death. Despite PDT has been approved for clinical practice and it is currently used for the treatment of some diseases, its application is not yet widespread [1]. Some limitations prevent the use of PDT in deep-tissues; especially the poor transparency of biological tissues makes it difficult to reach the interested sites with a suitable amount of light. Side effects due to systemic drug administration, such as induced toxicity upon exposure to natural light, are also a limiting factor to the use of some PDT protocols. Therefore, local delivery of photosensitizers is highly desirable.

In order to develop a minimally invasive device, aimed for the parallel delivery of a photosensitizer and an adequate light source, our research group has been developing a hollow resorbable fiber based on an optically transparent, water soluble, biocompatible Calcium-Phosphate Glass (CPG) [2,3]. CPG-based compositions proved to be suitable for the fabrication of optical fibers and hollow fibers, showing enhanced optical properties compared to polymeric materials [4,5,6].

In this work, we present and discuss the results on the release mechanisms of molecular drugs (Theophylline, Procaine, Salicylic Acid, Caffeine) having different chemical-physical profiles. The drug release kinetics have been correlated with the interaction between the ionized molecule and the internal glass surface of the hollow fiber.

These results were useful to assess the behavior of the fiber's internal surface and pave the way towards controlled release of more complex molecules, such as photosensitive drugs for PDT. Further research is ongoing in this direction. We will present preliminary results obtained on the controlled release of Rose Bengal and Methylene Blue upon different local and surface conditions and hollow fiber processing.

2. Experiments and results

The phosphate glass used in this work was synthesized according to a previously developed procedure [3]. The hollow fiber was fabricated by drawing a tube-shaped 12 mm outer diameter preform, obtained by rotational casting. This technique enabled the fabrication of about 150 m of fiber, with external and internal diameters of 220 and 110 μm , respectively. Optical microscopy analysis on different hollow fiber sections revealed a good quality of the material with constant outer ($\pm 3 \mu\text{m}$) and inner ($\pm 6 \mu\text{m}$) diameters. A typical picture of the cross-section of the hollow fiber, is depicted in Fig. 1a. IR camera observations were used to evaluate the light guiding in the fiber. The IR pictures acquired on the fiber tips, confirmed the guiding of the light in the wall of the hollow fiber along a length of 60 cm, due to total internal reflection (Fig. 1b). A dissolution test in Phosphate Buffered Saline solution (PBS, pH = 7.4, T = 37 °C) was carried out on 1.5 cm-long sections of the hollow fiber. The results confirmed the solubility of the glass in aqueous media, as the hollow fiber underwent complete dissolution within 21 days with a maximum pH reduction of 0.3 throughout the test.

A set of release tests were performed with Procaine, Salicylic Acid, Caffeine and Theophylline, to investigate the interaction between the glass surface and the molecules in cationic, anionic, and neutral state, at physiological pH.

We filled 2 cm-long sections of the hollow fibers by dipping them for few seconds into a solution of PBS and the selected drug (20 mM). The drug release was monitored in clean PBS by UV-Visible (UV-Vis) spectroscopy. The absorbance of the characteristic peaks of the drugs in the 200 – 300 nm region was measured every three minutes until complete release. The concentration of the released drug was finally obtained by interpolating the appropriate calibration curve [5]. The same procedure was repeated using a solution of Methylene Blue (2 mM) in PBS and a solution of Rose Bengal (9.4 mM) in ethanol.

The time evolution of the drug release revealed the occurrence of an interaction between the glass inner surface and the investigated molecules, especially in the presence of molecules at the ionic state in physiological conditions (Salicylic Acid and Procaine). These drugs appeared to interact with the surface of the glass by hydrogen bonding or dipole interaction, therefore withholding more than neutral molecules [5]. The release experiments showed also a strong interaction between the Methylene Blue and the glass surface, leading in this case to an incomplete release of the drug.

The analyses on the release of Rose Bengal exhibited a constant release kinetics and a complete release within 15 min (Fig. 1c). The released drug diffused homogeneously in clean PBS and its concentration could be easily measured (Fig. 1d). Intensive studies are currently ongoing and the dispersion of the measurements is under evaluation. The results will be presented at the Conference.

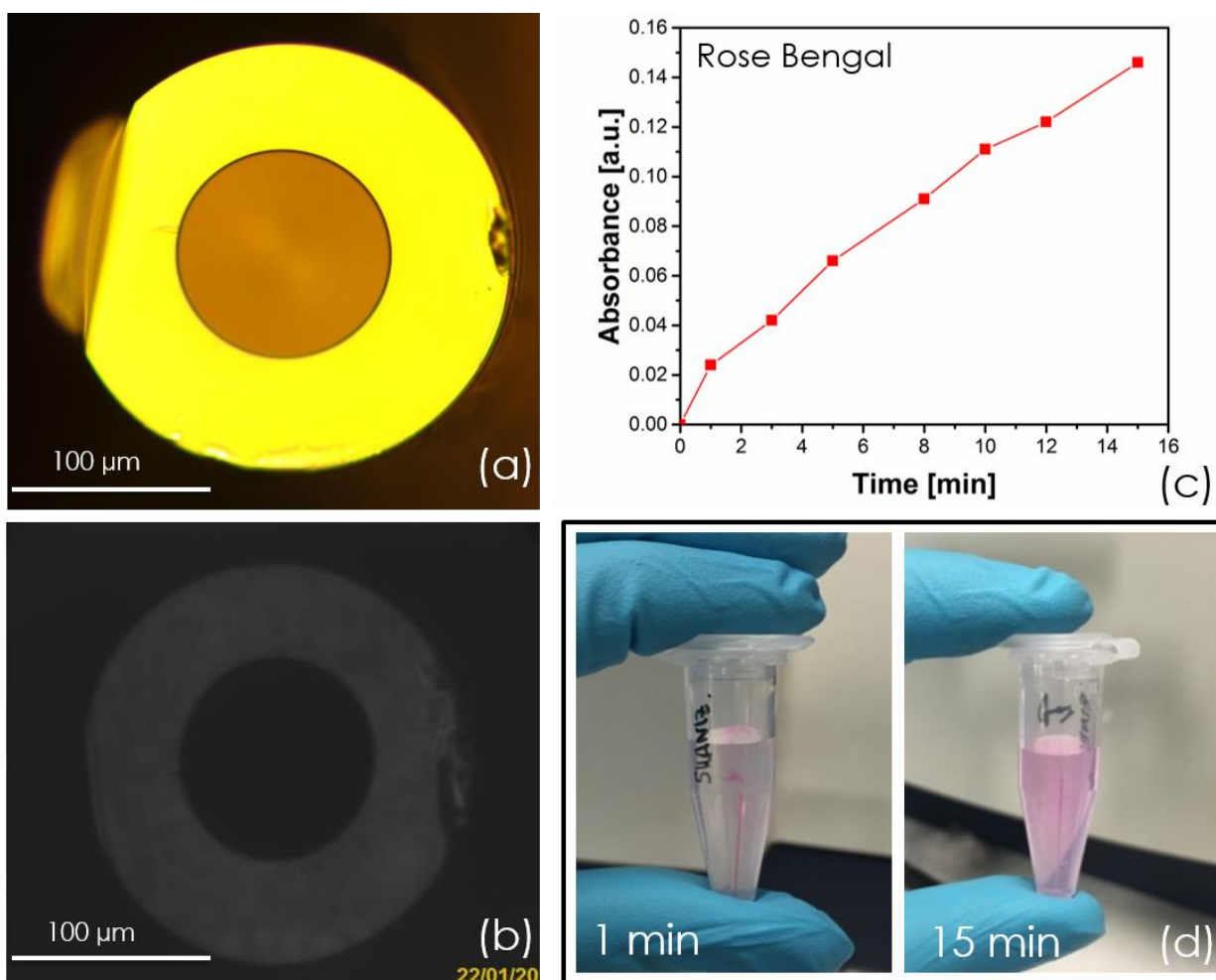


Fig. 1. (a) Optical microscope micrograph of the hollow fiber cross-section. (b) IR picture of the cleaved fiber tip, showing 1300 nm wavelength light being guided in the fiber's wall. (c) Typical release pattern of a sample of hollow fiber filled with Rose Bengal in PBS. (d) Capillary filled with Rose Bengal immersed in clean PBS for the release test.

4. Conclusions and future perspectives

Resorbable and optically transparent materials can enable the development of novel minimally invasive solutions for photo-induced therapies, e.g., photodynamic and photo-thermal therapies. In this work, the combined delivery of a photosensitive dye and the correspondent light excitation source, was demonstrated within the same device. The developed device consisted of a resorbable calcium phosphate glass hollow fiber. Additionally, the interaction mechanism between the inner surface of the fiber and the investigated molecules has been studied with the aim of optimizing their release kinetics. Further developments can be achieved improving the design of the fiber section. More complex hollow fiber designs can potentially improve the control of drug delivery and light guiding, limiting the device's optical losses.

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