PMMA/Graphene drug delivery systems as promising candidates for intraocular devices to improve glaucoma surgery

Mónica Machado[1], Gabriela A. Silva[1, 2] , Joana T. Ferreira[3, 4], Quirina Ferreira[2,5]

[1]Nova Medical School/Faculdade de Ciências Médicas, Universidade Nova de Lisboa, Campo Mártires da Pátria 130, Lisbon, Portugal
[2]iNOVA4Health, CEDOC Chronic Diseases Research Center, NOVA Medical School, Universidade Nova de Lisboa, Campo Mártires da Pátria 130, Lisbon, Portugal
[3]Ophthalmology Department, Centro Hospitalar Universitário de Lisboa Norte, Lisbon 1649-035, Portugal
[4]Visual Sciences Study Center, Faculty of Medicine, Universidade de Lisboa, Lisbon 1649-028, Portugal
[5] Escola Superior de Tecnologia da Saúde de Lisboa
Av. D. João II, lote 4.69.01, 1990-096 Lisboa

A2021086@nms.unl.pt

Abstract

Glaucoma is one of the major causes of blindness and in late stages it requires surgery. There are several glaucoma surgery techniques, for example, a common approach involves the application of an implant (valve) to drain the aqueous humor. However, postoperative wound healing produces an exacerbated response from the fibroblasts, clogging the introduced drainage canal [1]. Due to that, the development of new drug delivery systems have been receiving great attention in recent years due to its application to avoid the fibroblast proliferation without human intervention [2, 3]. The challenge is to develop biocompatible materials that do not affect the vision of the patients.
PMMA is a synthetic polymer that has arisen great interest in the biomedical field mainly due to its biocompatibility, transparency, high resistance to sunlight exposure and good optical properties [4, 5, 6].
The present study describes the development of a nanostructured smart drug delivery film adsorbed in thin substrates of PMMA that will be attached at the top of the glaucoma drainage device. This technique was applied by Mónica et al. in a recent study to develop a nanostructured and time-controlled film to release precise amounts of brimonidine (drug to control the Intra Ocular Pressure) at specific periods of time [7]. The presented multilayered films will be able to release precise amounts of the antimitotic drug 5-Fluorouracil (5-FU) used to control the fibroblast proliferation during the cicatrization time (one month) in postoperative glaucoma's surgery at specific periods of time.
The thin substrates of PMMA were made through drop cast method, dried and sterilized under UV light (figure 1).
Biocompatible films were composed of drug delivery layers and barrier layers. The drug delivery layers had 5-FU encapsulated in β-cyclodextrin (β-CD) to promote the solubility and reduce the toxicity of the drug. The barrier layers were made of a hydrossoluble polymer (poly (β-amino ester)) and graphene oxide [8, 9], to delay and control the drug's release. The drug delivery layers were alternated adsorbed with the barrier layers by the layer-by-layer assembly (LBL). LBL as a simple and versatile technique that allows to control the architecture of the film and can be repeated as many times as the desirable layers. The growth of the film was monitored by ultraviolet-visible spectroscopy. The acquired results demonstrated that the films are stable on the PMMA substrate with a perfectly linear increase of the absorbance intensity with the adsorbed layers (figure 2). These results are in concordance with the ones achieved in a previous study where it was used quartz substrates (figure 3.) In that study it was also showed that the presence of graphene oxide and a hydrossoluble polymer can control the drug release (figure 4). Specifically, it was shown that graphene oxide significantly slows the release of 5-FU, allowing for exact control of the dosage administered. This work helped to advance the creation of new drug delivery films in a biocompatible PMMA substrate, that can be applied to enhance the recovery of glaucoma surgery.

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Figures

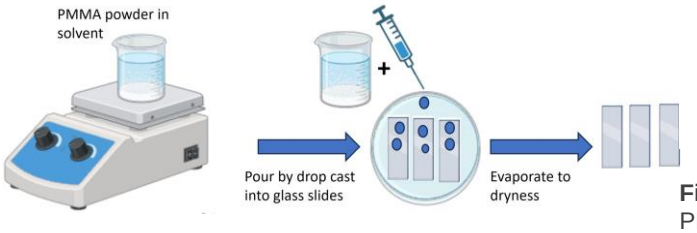

Figure 1. Fabrication of PMMA substrates by drop cast.

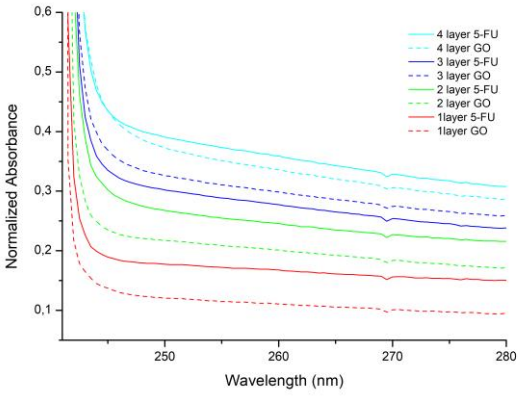

Figure 2. Normalized absorbance spectra of drug delivery film growth in PMMA substrate, representing that film layers are stable and grow sequentially.

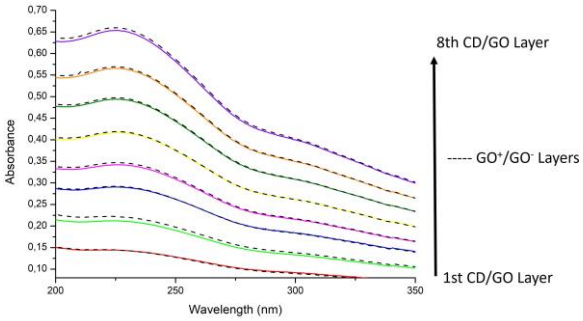

Figure 3. Absorbance spectra of drug delivery film growth representing that film layers are stable and grow sequentially.

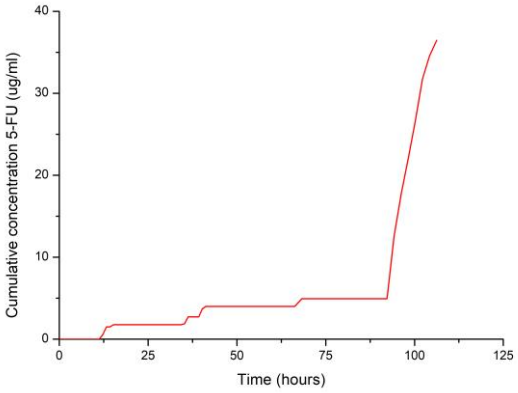

Figure 4. Cumulative concentration release of 5-FU in PBS solution over time.