Mathematical modelling of variable porosity coatings and dual drug release

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Abstract

The topic of controlled drug release has received much attention in recent years, for example in the design of tablets and in local drug delivery devices such as stents, transdermal patches, therapeutic contact lenses and orthopaedic implants. In recent years, we have developed a series of models for such devices to describe drug release from a polymeric platform, drug transport in surrounding biological tissues and fully coupled models of them. These works have culminated in the development of the first mathematical model to demonstrate agreement with in-vivo drug release and tissue uptake data, for the case of a drug-eluting stent [1].

If, on the one hand, these fully coupled models are indeed necessary to understand the spatio-temporal drug concentration in the surrounding environment, on the other hand it is clear that device manufacturers cannot intervene on the underlying biology. What they can control, however, are the properties of the polymeric platform to ensure the desired drug release profile is achieved. Indeed, the release profile is known to be a key predictor of device performance. Therefore, in the present work we take a step back from the fully coupled computational models and focus instead solely on the properties of the drug-containing coating.

We consider two particular aspects of the drug coating design. Firstly, the delivery of two therapeutic agents, what we refer to as dual drug delivery. Depending on the particular application in question, it may be desirable for the drugs to be released at similar rates, or perhaps one of the drugs released rapidly with the other being eluted over a longer period of time. In the case of drug-eluting stents, for example, devices which release an anti-proliferative and a 'pro-healing' drug have been proposed, whilst a combination of two of the early drug-eluting stent drugs - paclitaxel and sirolimus - has also been suggested. Secondly, motivated by today's advances in micro and nanotechnology, we propose variable porosity multi-layer coatings as an additional means of controlling the dual drug delivery.

In this talk we present our mathematical model of dual drug delivery from a durable polymer coated device. We demonstrate how the release rate of each drug may in principle be controlled by varying the underlying microstructure of polymer coating [2] or by altering the initial loading configuration of the two drugs [3]. Our results show the role of the relevant material parameters used to tailor the release curves to a given application.

References

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