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Microfluidic controlled and continuous drug delivery for dry eye disease treatment

Nanotechnologies
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Abstract

In this work we have developed a device (10 x 5 mm, rectangular shape) for controlled delivery of drugs to the eye consisting of a 320 µm hyaluronic acid (HA) laden hydrogel covered on one side by a monolayer of graphene, added to allow slow release of the active component and acting as an impermeable layer. The HA was tested at 0.5, 1, and 2 % w/v, and was used due to its lubricating and wound healing properties. Three inserts were tested on a healthy dog after written informed consent from the owner, via placement in the cul-de-sac of one eye with the graphene layer facing the outer eyelid. The first two inserts remained positioned in place for ~6 h each until expulsion while the third insert only for ~1 h. Results show good biocompatibility, with needed biofunctionality gain to increase dwell time.

Methodology

- HEMA (2-hydroxylethylmethacrylate) based hydrogel fabrication was tested with 3 methods: spin coating; wetting and spreading; and casting, using different concentrations of HA (hyaluronic acid).
- Graphene was grown by CVD (chemical vapour deposition, Fig.1) on copper foil to achieve high purity graphene monolayer, with small amount of defects. The graphene was then transferred by wet transfer onto the hydrogel. The device was cut to dimension with cutters developed in-house (Fig.2).
- In vivo testing was done in a small Podengo breed dog (Fig.3), with HA laden Hydrogel (shape B), HA laden Hydrogel/Graphene (shape C) and HA laden Hydrogel/Graphene/PMMA (polymethylmethacrylate) (shape B).

Results

- Hydrogel casting with 0.5 % w/v HA gives best thickness uniformity and structural integrity
- Good response for biocompatibility *in vivo*, with dwell times up to 6 h before being expelled. Slight increase in clinical signs of conjunctivitis for insert HA laden Hydrogel/Graphene/PMMA
- Further optimization is needed to reduce dimensions of the device to improve biofunctionality

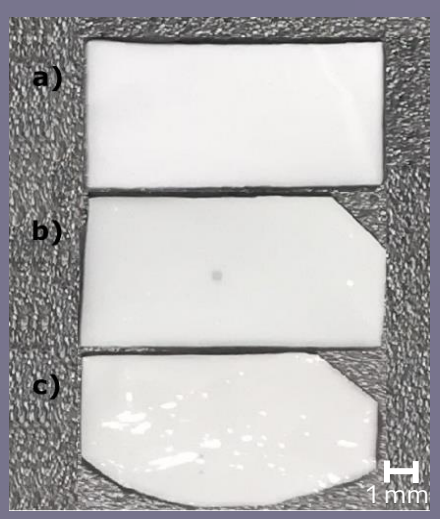

Fig.2 Devices with different shapes

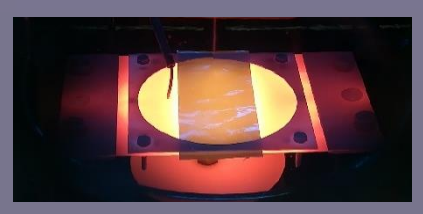

Fig.1 Graphene growth by CVD

Fig.3 *In Vivo* cul-de-sac placement

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