Optimisation of cold atmospheric plasma (CAP) process parameters for deposition of paclitaxel in ethanol/water as a drug coating on angioplasty balloons.

Ethan Morrissey[1,2], Liam O'Niell[2], Abina Crean[1], Katie B. Ryan[1]

[1] School of Pharmacy, University College Cork, College Road, Cork, Ireland.

[2]TheraDep Ltd, Ballingarane, Clonmel, Co. Tipperary, Ireland.

Background:

Arteries can become blocked over time with fatty deposits, leading to stenosis. When these blockages become severe in the blood vessels that supply blood to the heart, a heart attack can occur. Angioplasty balloons are medical devices used in revascularization procedures to re-open stenotic arteries. This involves inflating a balloon to stretch the plaque and restore blood flow to tissue downstream of the stenosis. An anti-proliferative drug is transferred to the plaque during the time that the balloon is inflated, to minimize re-stenosis. However, short inflation times significantly hinder drug transfer, necessitating high drug loadings to ensure a therapeutic dose is delivered. Furthermore, drug loss due to abrasive forces removes the drug from the balloon prior to contact with the plaque. The aim of the research is to determine the optimum cold atmospheric plasma coating parameters, namely coating chamber length and atomization pressure to deposit uniform paclitaxel drug coatings.

Methods:

This research utilised TheraDep's BioDep cold atmospheric plasma process to produce coatings on glass slides. A full factorial design of experiments approach was used to determine the effects of different process parameters on the drug coating produced. These included the coating chamber length (22, 33, and 44 mm) and the nebulizer pressure used for atomization of the coating solution (2, 3, and 4 bar). Paclitaxel was coated on glass slides at a concentration of 7.5 mg/ml for a duration of 8 seconds using ethanol:water (8:2 v/v) as the paclitaxel solvent at a flow rate of 100 µL/min.

The coatings deposited were analysed using polarizing microscopy and atomic force microscopy (AFM). The amount of drug deposited was quantified using HPLC.

Results:

Polarising microscopy revealed that all the coatings produced with the 22 mm chamber appeared to have higher levels of crystallinity, compared to the longer chambers, with the exception off samples deposited using the 33 mm chamber at a pressure of 2 bar. AFM analysis revealed that the nebuliser pressure did not have a statistically significant effect on the coating roughness for samples deposited using the 22 mm chamber. However, ANOVA analysis showed some of the coatings deposited using the 33 mm and 44 mm chamber groups had significant differences between them. Studies to quantify drug deposition are ongoing.

Conclusions:

This work suggests that the nebulizer pressure has a significant impact on the coating roughness when longer chambers are used, and that the chamber length has a more meaningful effect on the coating crystallinity than the nebuliser pressure.