

Abstract

Dexamethasone and ciprofloxacin release and bio-efficacy after autoclavation of 3D printed external ear canal implants

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Patients with chronic stenosis of their ear canal may benefit from additively manufactured individualized drug containing external ear canal implants (EECI) [1] that keep the ear canal open and support the healing of the affected tissue. To guarantee the safety of the patients, the sterilization of implants is important. Autoclaving is a fast and well-established sterilization method, but the heat of the process may damage any drug contained within the implants. To evaluate the suitability of autoclaving EECIs, we tested samples for bio-efficacy and the released drug amount within 3 days.

Three EECIs were 3D printed with an EnvisionTEC Bioplotter (Manufacturer Series, Desktop Metal, Burlington, USA) using UV-Silicone 60A MG (Momentive, Niskayuna, USA) [1] loaded with 1 (w/w) % dexamethasone (DEX, caelo, Hilden, Germany) and 0.3 (w/w) % Ciprofloxacin (Cipro, Sigma Aldrich, Hamburg, Germany). Samples were autoclaved with a Lisa Remote Plus Sterilizer (W&H, Bad Reichenhall, Germany) at a maximum temperature of 134°C for the duration of 350s. Next, the samples were incubated at 37°C for 72 h in isotonic sodium chloride solution (0.9 (w/v) % NaCl, 1 ml NaCl per 0.2 g sample). For the analysis of released drug content within the incubated NaCl, an Ultra High Precision Chromatograph (Xevo Qtof MS, Waters, Germany) coupled with a time-of-flight micro-mass spectrometer (Q-TOF, Waters) was used [2]. The bio-efficacy was assessed using a TNF α (tumor necrose factor- α) reduction assay [1], pure DEX (35,33 μ g/ml) served as positive control.

12.94 $\pm$ 0.29 μ g/ml of DEX and 1.67 $\pm$ 0.06 μ g/ml Cipro were released from the samples within 72h. The TNF α production was reduced by 80.66 $\pm$ 0,02 % (pure DEX) and 58.45 $\pm$ 0,10 % (sterilized samples).

Since the supernatant of the sterilized samples induce TNF α reduction it can be concluded that an effective amount of DEX survives the autoclaving. The bio-efficacy of the released ciprofloxacin will be evaluated via a zone of inhibition test. Overall, autoclaving may be used to sterilize DEX- containing 3D printed silicone implants. Whether the samples will have a therapeutic effect in the patient will have to be shown by future studies.

AUTHOR'S STATEMENT

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