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SILICONE-HYDROGEL-COMPOSITE FOR CELL BASED THERAPIES: A NOVEL SILICONE BASED IMPLANT MATERIAL FOR IMMOBILIZATION OF DRUG RELEASING CELLS

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CONTEXT

The insertion of implants bears the risk of foreign body reactions like inflammation or fibrosis. To prevent this as well as to promote required biolocal activity, cell based drug delivery systems might be used, in which cells provide a sustained supply of drugs. Alginate is a suitable encapsulation matrix for those systems, but as it lacks a chemical fixation to the implant material, cell containing alginate coatings are sensitive to strain.

A novel composite consisting an interpenetrating network (IPN) out of silicone and alginate may overcome these problems. It is a flexible material (Fig. 1) in which the alginate network is mechanically anchored in the silicone.

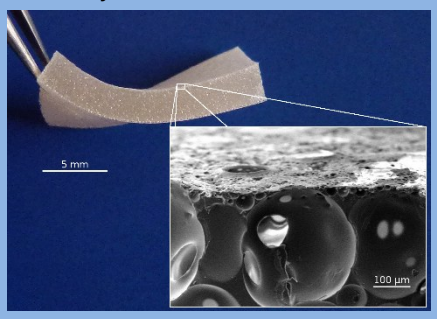

Fig. 1: Elastic silicone-alginate-composite with connected pores inside the composite (detail SEM image)

AIM

The aim of this study was to reveal the potential of the silicone-alginate-composite as a biocompatible matrix for cell based drug delivery systems.

METHODS

- Preparation of composites with different amounts of alginate
- Water contact angle measurements on cross sections
- Pore size measurements of the IPN (by SEM)
- Cytotoxicity tests (BrdU, WST-1) of composites with low (lmw) and high molecular weight (hmw) alginate
- Long term evaluation of L929-fibroblasts immobilized for 25 days inside the alginate phase of composites with sizes of 5x5 mm² and thicknesses of either 1, 2 or 3 mm.

RESULTS

Composites with hmw alginate revealed close to 100 % viability and those with lmw alginate slight cytotoxicity (WST-1: 69%; BrdU: 80%).

The composites showed reduced hydrophobicity with contact angles < 75° and pore sizes of about 150-180 µm (Fig. 2, Tab. 1).

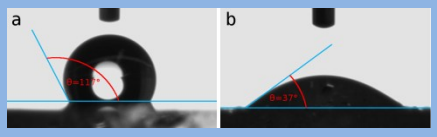

Fig. 2: Water contact angle of pure PDMS (a) and a composite with 80% alginate content (b)

Tab. 1: Pore sizes and water contact angles of PDMS and composites depending on the alginate content

Alginate content [%]	Pore size [µm]	Contact angle [°]
70.0	178.9 ± 42.4	74.6 ± 18.9
75.0	225.9 ± 44.9	54.8 ± 10.3
80.0	245.8 ± 47.6	44.0 ± 11.1

Embedded L929 cells proliferated quickly and formed multicellular spheroids within the composite (Fig. 3).

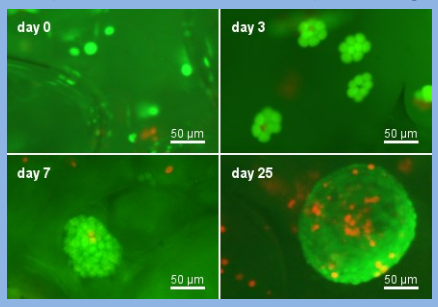

Fig. 3: Inside the composites embedded and immobilized L929 cells growing to multicellular spheroids with time

About 40% of all cells were still living after 25 days (Fig. 4). They were mainly located at the composites' boundary area.

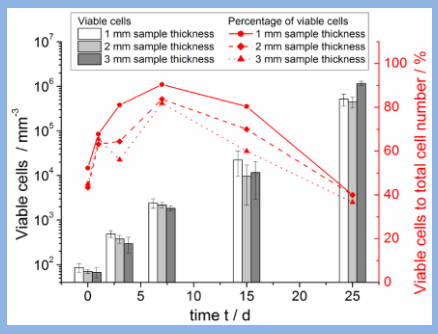

Fig. 4: Long term survival of L929 fibroblasts immobilized in composite samples of different thicknesses

SUMMARY AND CONCLUSIONS

The novel silicone-based composite is hydrophilic and shows no cytotoxicity when composed of high molecular weight alginate.

Depending on the alginate content, the composite contains pore sizes big enough to embed cells into the alginate phase. In such a way immobilized L929 cells were able to survive and proliferate over of 25 days.

The composite is suited to be used as flexible implant material, in which drug releasing cells can be immobilized to continuously release biologically active substances.

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