ABSTRACT SUMMARY
A novel hybrid material consisting of silicone rubber and hydrogel is being developed. It is found that this hybrid material can be loaded with a wide range of drugs and show controlled release for several weeks. Here the antimicrobial effect of the hybrid material when loaded with silver lactate is reported.

EXPERIMENTAL METHODS
In a typical experiment a 16 mL stainless steel high-pressure reactor equipped with pressure transmitter is loaded with silicone elastomer samples, 4.00 mL EtOH, 2.00 mL HEMA and 60.0 µL EGDMA in the giving order. The reactor is closed, placed in a water bath at 75° C and pressurized with CO2 to approx. 250 bars under stirring. After approx. 25 min. 500 µL 0.20 M DEPDC in hexane is injected through an HPLC loop by increasing the pressure to 360 bars. After the polymerization step (approx. 2.5 h) the pressure is slowly released over 20-30 min. The produces IPN samples are collected and cleaned in water and dried until constant weight before the hydrogel content is determined by weighing.

The produced IPN samples are loaded with drugs by adding approx. 100 mg silver lactate and 1.60 mL 99% EtOH to a 16 mL stainless steel reactor equipped with a magnetic stirring bar and a grid. After stirring for approx. 20 min two IPN samples are added and the reactor is closed and pressurized with CO2 under stirring to 100 bars at room temperature. Then the temperature is increased to 75° C. After 24 hours the pressure is slowly released.

Network morphology in IPNs is illustrated by loading the IPNs with fluorescein and analyzing with laser scanning confocal microscopy (LSCM).

The antimicrobial effect of samples loaded with silver lactate i. Method I, the IPNs are placed on an agar plate and a top-agar containing E. coli is poured across the surface. The agar plate is incubated at 37° C for 24 hours. Method II, after ETO sterilization the samples are immersed in artificial urine solution inoculated with approx. 1x10^5 vancomycin resistant enterococci (VRE). The samples are incubated at 36° C. After day 3 and 7 the following three assays were performed: Planktonic growth of the contacting solution
RESULTS AND DISCUSSION

IPNs with different hydrogel contents are placed in an aqueous fluorescein solution for two weeks. By applying this method only surface connected hydrogel material will contain fluorescein and hence give a signal. The samples are examined with LSCM to analyze the network morphology, see Figure 1.

![Figure 1. LSCM analysis of IPNs with A:10%, B:18% and C:26% hydrogel loaded with fluorescein. Scale bar corresponds to 5µm.](image)

It is obvious from figure 1 that the network morphology is dependent on the hydrogel content. When the hydrogel content is low there is an increased risk of entrapping the hydrogel material in the silicone due to clustering of hydrogel, see Figure 1A. As the hydrogel content is elevated the surface connectivity increases and a higher proportion of hydrogel becomes accessible for drug loading. IPNs containing 25% hydrogel are used for testing the antimicrobial properties of IPNs.

![Figure 2. Agar plate from experiment with silver lactate incubated at 37°C for 24 hours. In the upper part two IPN samples loaded with silver lactate is placed and in the lower part an untreated silicone elastomer sample is placed.](image)

Figure 2 shows the agar plates with *E. coli* from method I after incubation. Clear zones of inhibitions are observed around the two IPNs loaded with silver lactate. No zone of inhibition is observed at the reference sample in the bottom of the agar plate; an untreated silicone elastomer.

Table 1 lists the results of the antimicrobial effect evaluated by method II. The antimicrobial effect of IPNs is compared to that of silicone elastomers without hydrogel. Both sets of samples are loaded with silver lactate.

<table>
<thead>
<tr>
<th>Sample</th>
<th>Day 3</th>
<th>Day 7</th>
<th>Growth</th>
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<tbody>
<tr>
<td>IPN</td>
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Table 1. Antimicrobial effect of IPNs and silicone elastomer loaded with silver lactate against vancomycin resistant enterococcus. CS denotes the planktonic growth of the contacting solution. S denotes the count of attached viable cells on the samples.

As seen from table 1 there is no growth of VRE in the experiments with IPNs. Whereas the silicone elastomers loaded with silver lactate show growth of VRE in the contact solution and on the samples both at day 3 and day 7.

CONCLUSION

IPNs of silicone rubber and PHEMA produced in scCO2 can be effectively loaded with silver lactate. It is further found that the loaded IPNs show antimicrobial activity toward *E. coli* and vancomycin resistant enterococcus. This makes IPN loaded in scCO2 a candidate for further studies into design of long term drug release systems.

REFERENCES