Silicone Based Nanocomposite for Treatment of Hydrocephalus

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Statement of Purpose: Cerebrospinal fluid shunts commonly molded from silicone rubber are widely used for the treatment of hydrocephalus (abnormal fluid build-up inside the brain). Continuous research and improvements have been made to the shunt system over the last few decades; nevertheless, the problems of shunt complication and failure continue to be a serious issue. Obstruction by tissue and infection by micro-organisms are two major causes of failure of silicone shunts. These problems led us to the development of new material for shunt applications with high antimicrobial and antiproliferative activity. Based on the preliminary studies our hypothesis is that silicone with silver-clay nanohybrid structure and paclitaxel together provides highly effective and sustained broad-spectrum antimicrobial and antiproliferative activity required to significantly reduce malfunction of silicone shunts caused by obstruction and bacterial infection.

Methods: The process for in-situ precipitation of silver in clay surface involved the following: Prior to the precipitation of silver nanoparticles on the clay surface, clay (montmorillonite (MMT)) was ball milled for 60 min to break the individual tactoids. Briefly, 1.0 g of MMT nanoclay (PGN or I.44P) was added to 100 ml of 0.02 M silver nitrate solution and stirred vigorously for 30 min, while being heated at 60°C for 8 h. The resulting mixture was centrifuged at 5000 rpm and washed with distilled water. The container was wrapped with aluminum foil and the reaction carried out in a dark room. The reduction process involved reduction with sodium borohydride (0.04 M). After the end of the reduction reaction, Ag-clay nanohybrid was washed several times with water. Antimicrobial activity of the silver-clay nanohybrid was investigated using Escherichia Coli (ATCC29181). Preparation of bacterial culture is described elsewhere (1).

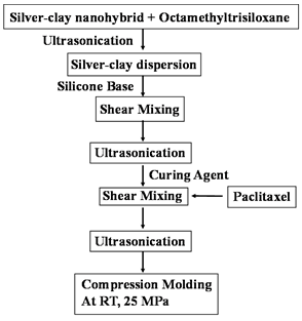

Figure 1. Flow chart illustrating the fabrication of hybrid silicone with silver-clay nanohybrid and paclitaxel.

Results: Hybrid silicone showed excellent mechanical properties i.e. enhancement of strength and retention of high elongation compared to stand alone silicone. The simultaneous attainment of high tensile strength and large elongation in silicone is significant and desired result to not only prevent mechanical failure but also allow reduction in outer diameter of the shunts.

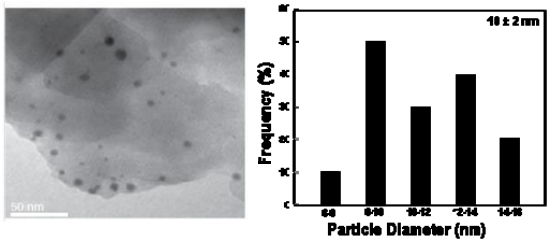

Figure 2. Transmission electron micrograph and particle size distribution of silver precipitated on the clay surface fabricated by chemical reduction process.

Figure 2 shows that in-situ precipitated silver nanoparticles on clay were significantly smaller and uniformly dispersed. It is elucidated that the synergetic effect of silver-clay nanohybrid is to provide a diffusion-controlled and effective antimicrobial activity. Results from antimicrobial activity tests showed that the number density of E. Coli bacterial colony decreased by ~ four orders of magnitude as compared to bare silver, which indicates superior antimicrobial performance.

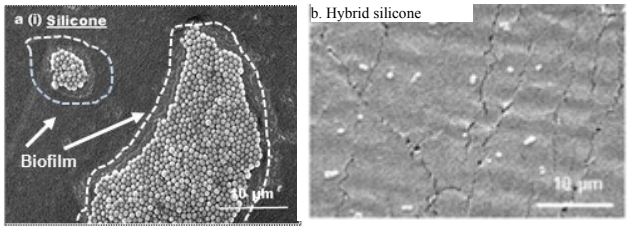

Figure 3. SEM micrographs illustrating the adhesion and colonization of S. aureus on silicone elastomer on (a) pure silicone and (b) hybrid silicone.

Figure 3 shows significant reduction in bacterial colonization of S.aureus on hybrid silicone.

Conclusions: The effective and enhanced antimicrobial activity of silver-clay nanohybrid structure is attributed to the large surface area and homogeneous dispersion of silver nanoparticles on clay platelets. Based on preliminary studies, we have developed a longer lasting solution to significantly reduce both cell growth and bacterial infection. The approach to reduce bacterial colonization involves the incorporation of novel silver-based nanoclay in silicone in a manner to obtain higher antimicrobial efficiency and homogenous protection of silicone shunt surface. On the other hand, to reduce growth, impregnate silicone with antiproliferative paclitaxel. The unique and controlled antimicrobial properties of silver-clay nanohybrid and antiproliferative characteristic of paclitaxel would make them ideal materials in silicone for dual-action of effectively reducing infection and cell growth.

References: (1) Girase B, Depan D, Shah JS, Xu W, Misra RDK. Mater Sci Eng C. 2011; 31; 1759-1769.