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The effect of hexetidine and triclosan on the curing and mechanical properties of silicone elastomer

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Silicone is a biomaterial that is commonly employed in the fabrication of medical devices and drug delivery systems. In the latter, the inclusion of therapeutic agents is performed prior to the cross-linking process. The mechanical properties of the final device are important determinants of clinical performance, affecting properties such as drug release, resistance to fracture and ease of insertion (Gorman et al. 1997). However, there is little information available concerning the effects of therapeutic agents on the mechanical properties of silicone biomaterials. Therefore, this study reports the use of a dynamic mechanical method to characterise both the cross-linking process and, also, to quantify the mechanical properties of the final product. In addition, the effects of two antimicrobial agents, hexetidine and triclosan, selected for medical device applications, on these properties are reported.

Elastomer base (Med-6383, Nusil, USA) and cross-linking agent (tetrapropoxysilane) were mixed in a ration of 100:2.5 parts by weight. Hexetidine (0 - 1% w/w) or triclosan (0-5% w/w) were incorporated with mixing into this system. Cross-linking was initiated by the addition of catalyst (stannous octanoate, 0.5%w/w), at which point, dynamic analysis of the mixture was commenced. All analyses were performed at 1.0 Hz and 20°C using compression plate geometries (1mm plate separation). Cross-linking was followed by measuring the rate of increase in storage modulus (G'), a measure of rigidity, as a function of time, and the time required, and magnitude of G' at equilibrium. The effects of hexetidine and triclosan on these parameters was statistically evaluated using a one-way ANOVA ($p<0.05$).

% Drug	Rate of curing	Max. G'	Time to
0.00	1599.03	491.9±16.6	800
Hex. 0.50	884.58	436.4±9.5	1200
0.75	726.03	392.1±6.3	1000
1.00	25.94	53.2±7.4	2500
Tric. 1.00	545.08	457.4±12.0	3000
2.00	528.03	453.5±12.3	3000
5.00	80.53	342.0±6.4	5600

Table 1. Effects of hexetidine and triclosan on the rate of curing, time required for and equilbrium values of G'.

In the absence of hexetidine or triclosan, cross-linking proceeded immediately, continued for *circa* 750s until a plateau in G' was observed (491.9±16.6kPa), indicative of completion of cross-linking. In the presence of hexetidine or triclosan, both the rate of curing of the silicone biomaterial and G' at equilibrium were significantly decreased, whereas the time required to reach the plateau in G' was significantly greater in comparison to the drug-free silicone. Interestingly, in the presence of hexetidine (1% w/w), the general profile of G' against time was significantly altered and consequently, no sharp initial rise in elasticity was observed but instead G' increased gradually. This is reflected in the large time required to achieve an equilibrium G' and also in the low rate of curing of this biomaterial. Furthermore, in the presence of triclosan (5% w/w), the onset of curing was delayed by *circa* 1000s), after which time, the rate of curing, the equilibrium G' and time to reach equilibrium were significantly lower than drug-free silicone.

Therefore, this study has shown that the therapeutic agents employed in this study significantly affected the cross-linking reaction involved in the formation of silicone. Thus, both the rate of reaction and the elasticity of the final product were significantly reduced. In light of the structure of the drugs employed in this study, it is suggested that these observations are not a result of direct poisoning of the catalyst. However, it is suggested that the presence of triclosan as a suspended solid results in physical inhibition of the catalyst thus producing regions of lower cross-link density and a less regular network structure. Conversely, the more pronounced effects of hexetidine on cross-linking may be attributed to molecular inhibition of the catalyst as this antimicrobial agent was freely soluble in both the uncross-linked and cross-linked materials.

In conclusion, this study has highlighted both the applicability of dynamic mechanical methods to assess cross-linking reactions of polymers and, also, the potential problems of drug inclusion into silicone biomaterials.

Gorman, S.P., Jones, D.S., Bonner, M.C., Akay, M., Keane, P.F. (1997) Biomaterials 18(20), 1379-1383.