 DOI: 10.1002/masy.201150313

Organo-Montmorillonite as a Controlled Release Reservoir for Triclosan in Silicone Elastomer: A Flow Micro-Calorimetry and Leaching Study

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Summary: Organically modified montmorillonite (o-MMT) in a room temperature addition cured silicone elastomer (PDMS) has been found to control the release of 2,4,2′-trichloro-2′-hydroxy diphenylether (triclosan (TCS)) from the composite. The effect of o-MMT gallery polarity on controlled release was investigated via different intercalants and the interaction of triclosan with the o-MMT was investigated using flow micro-calorimetry (FMC). The latter was found not to be a universal predictor of controlled release activity of the composite as combined TCS and PDMS interactions with MMT/o-MMT leading to intercalation (observed using WAXS) and controlled release activity must also be considered. Southern Clay Products Cloisite® 15A (C15A) gave the most sustained release of TCS whilst also featuring a uniform gallery spacing in the composite. A pore structure based on self-assembled C15A intercalant alkyl tails is tentatively proposed.

Keywords: antimicrobial; controlled release; montmorillonite; silicone elastomer; triclosan

Introduction

Colonisation of maxillofacial appliances (for example a voice prosthesis) by micro-organisms such as *Candida Albicans* is a major problem and can lead to both deterioration of the appliance [1,2] and infections such as oral candidosis in the patient. Direct addition of antimicrobials to a silicone elastomer formulation can lead to excessively fast release of the antimicrobial, hence rapid depletion to levels below the minimum inhibitory concentration (MIC), and therefore little long term advantage. Controlled release will lead to more sustained output of the antimicrobial, extended life of the appliance and a better quality of life for the patient. Attempts have been made to use gel silica as the controlled release reservoir.[3] In the latter case, the interaction with triclosan with silica was too weak [4] to afford an efficient controlled release effect under dynamic leaching conditions. The organophillic environment within the galleries of organically modified montmorillonite (o-MMT) may hold the antimicrobial more effectively, which combined with the high internal surface area could lead to improved controlled release performance. The purpose of this paper is to relate the effect of o-MMT type on the triclosan (TCS) leaching characteristics of silicone elastomer (PDMS)/TCS/o-MMT composites to o-MMT/TCS interactions (investigated by FMC) and to the combined effect of TCS/PDMS interactions with o-MMT in the composite (investigated by mechanical response and WAXS).

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Table 1.
Details of o-MMTs Used

MMT Type	Coding	Intercalant	Intercalant level (wt%)	Interlayer spacing (nm)
Cloisite® Na^+	CNa^+	None	zero	0.29
Cloisite® 30B	C30B	Methyl tallow* bis (2-hydroxyethyl) ammonium	24	0.82
Nanomer® I.3TC	NI.3TC	Octadecyl ammonium	29	1.49
Cloisite® 15A	C15A	Di(hydrogenated tallow)* dimethyl ammonium	39	2.41

Experimental Part

A range of o-MMT's (Table 1) were investigated together with NI.3TC preloaded with 20 g TCS (Ciba Irgasan® DP300) per100 g NI.3TC by toluene solution blending followed by evaporation of the toluene and micronisation of the resulting cake. Sodium montmorillonite (Cloisite® Na^+, (CNa^+)) was used as a control. The formulations were based on room temperature hydrosilylation cured silicone elastomer (PDMS) (Cosmesil Principality Medical Ltd.). The TCS was vacuum mixed with the silicone resin at 60 °C (this enabled melting of the TCS and hence improved dispersion) the catalyst and MMT was then added. For the leaching study the composites contained 3 wt% TCS and 11 and 15 wt% CNa^+ and o-MMTs, respectively, and for the WAXS and mechanical property investigation, composites contained 1.38 wt% TCS and the o-MMT level was adjusted such that the MMT silicate level was 5 wt% in all composites. 1.5 mm thick plaques were cast at room temperature from PMMA moulds. For the leaching study, squares (1 cm $\times$1 cm) were cut from the plaques which were then placed in deionised water (20 ml) and agitated at 37 °C. The concentration of TCS in the water was determined every three days by UV spectroscopy (at $\lambda_{max} = 198\,nm \pm 2\,nm$), the water was changed after each spectroscopic measurement. It should be noted that the unfilled control sample contained 1 wt% TCS as even at this level slight blooming of TCS crystals were observed on the surface of the moulding due to the insolubility of TCS in PDMS, a sample containing 3 wt% TCS would therefore not give meaningful data. The adsorption of TCS onto the o-MMTs was studied from heptane at 30 °C using flow microcalorimetry (FMC) the method is described elsewhere [5] but in summary, FMC enables heats of adsorption and desorption to be measured together with the associated amount of probe adsorbed and desorbed. The WAXS patterns (Cu-Kα) and tensile properties (BS903 type 2 dumbells, 200 mm/minute) of selected composites were examined in order to gain some insight in to the effect of TCS interactions on the dispersion of o-MMT platelets.

Results and Discussion

Figure 1 shows the effect of o-MMT gallery structure on the level of TCS adsorption at 30 °C from heptane as measured using the FMC. It is evident that C15A adsorbed TCS to a much higher level than the other o-MMTs. This was not due to swelling of C15A in heptane; in fact the level of swelling of C15A was low and similar to unmodified MMT (CNa^+). C30B and NI.3TC swelled in heptane to half the level observed with CNa^+ and C15A. The dominant hydrocarbon character of the gallery of C15A appears to favour compatibility with TCS, though perhaps more importantly the interlayer spacing is sufficient to accommodate the TCS molecule in a wider variety of orientations than the other MMTs examined.

The C15A containing composite gave by far the most sustained TCS release characteristic (Figure 2) followed by those

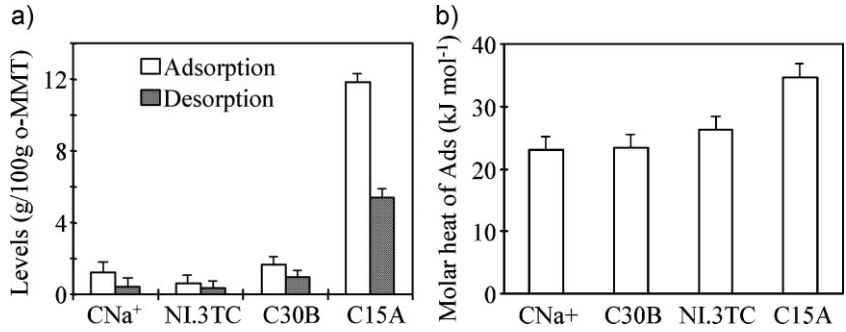

Figure 1.
Effect of MMT gallery structure on: (a) the level of TCS adsorption/desorption from heptane and (b) Molar heat of TCS adsorption.

containing NI.3TC, C30B and CNa^+. The fact that the latter two o-MMTs and the CNa^+ gave any controlled release at all implies that a greater surface area of MMT is available within the PDMS than in heptane during the FMC analysis. Therefore intercalation/delamination of MMT platelets in the PDMS may have occurred. Rapidly formed interactions between TCS and the o-MMT in the PDMS during mixing led to the release characteristics of the NI.3TC with in-situ added TCS and NI.3TC pre-loaded with TCS being identical.

Furthermore, during this study it was observed that addition of C15A clay significantly inhibited the cure of the PDMS; but that this inhibition did not occur on addition of C15A/TCS, this again confirming rapid adsorption of TCS from PDMS to an o-MMT. Even though no attempt was made to optimise the dispersion of MMT during the relatively low shear vacuum mixing of the composites, it was nevertheless considered worthwhile to examine the tensile properties (Figure 3). It is interesting that the CNa^+ based composite showed quite a noticeable increase in stress at 50% strain (M_{50}) relative to the unfilled matrix. However it is even more significant that addition of TCS to this composite led to increases in all measured mechanical properties relative to the equivalent composite containing no TCS. This observation points to enhanced intercalation/exfoliation and will be explored via WAXS. The o-MMT based composites show higher M_{50} than those

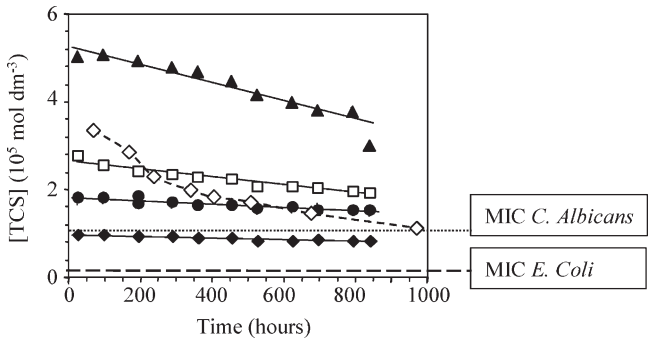

Figure 2.
TCS concentration versus time (water was changed after each reading) for formulations containing 3 wt% TCS: ▲ CNa^+, □ C30B, ● NI.3TC and NI.3TC pre-loaded with TCS, ◆ C15A. The open diamonds (◇), joined by a dotted line, denote 1 wt% TCS in PDMS.

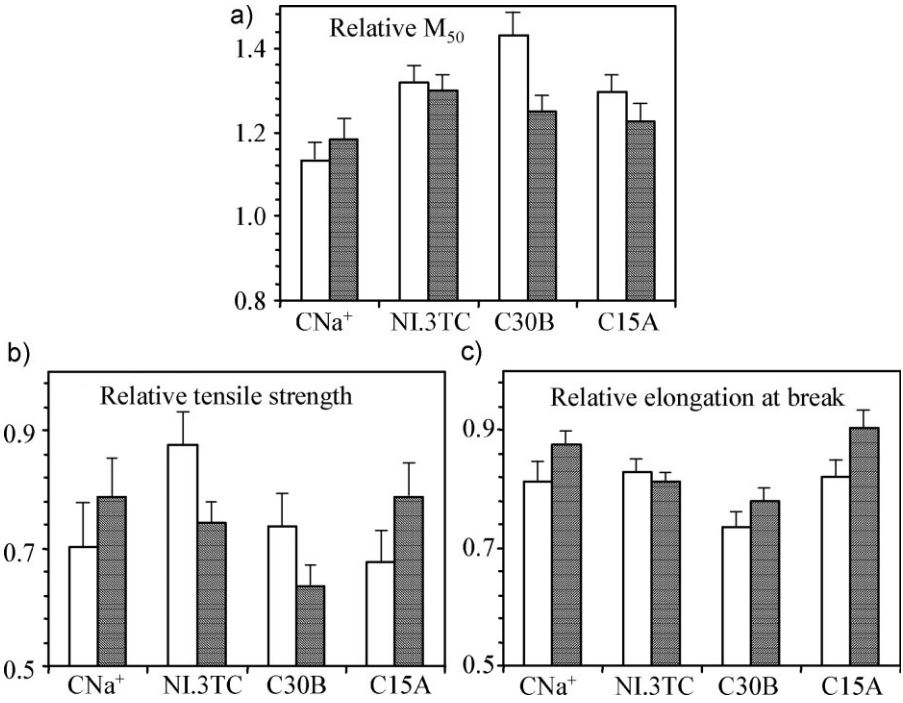

Figure 3.
Relative mechanical properties (to unfilled matrix) of PDMS/MMT composites (containing 5 wt% MMT): White bars and hatched bars represent composites without and with TCS, respectively, (a) M_{50}, (b) tensile strength and (c) elongation at break.

based on CNa^+; C30B gave the highest M_{50} and NI.3TC and C15A were equally slightly lower. On addition of TCS all the o-MMT based composites displayed a reduction in M_{50}; this was most noticeable with the C30B based composite and least noticeable with that based on NI.3TC. TCS resulted in reduced tensile strength (σ_f) of NI.3TC and C30B composites, but increased σ_f and elongation at break in C15A composites. The latter supports interaction between TCS and C15A that may lead to a reduction in the level of large C15A agglomerates.

WAXS data for the composites based on CNa^+ (Figure 4(a-ii)) reveal new reflection peaks at 1.75° (5.0 nm) and 2.4° (perhaps overlaid with the inherent PDMS reflection (Figure 4(a-iv)), indicating intercalation of a fraction of the CNa^+ present in the composite. Intercalation of Na-MMT by PDMS has also been noted by Keneko and Yoshida.[6] The reflection at 7.8° (1.13 nm), closely matching that for CNa^+ powder (Figure 4(a-i)), indicates a significant amount of non-intercalated CNa^+. Addition of TCS to the CNa^+ based composite resulted in further intercalation, producing disordered platelet stacks, as manifested by the sharp increase in counts below 2°. Interaction of TCS with the edge hydroxyl groups of CNa^+ may facilitate intercalation of PDMS and TCS. This proposition is supported by the enhancement of composite mechanical response on addition of TCS, and the noticeable controlled TCS release characteristics afforded by CNa^+ relative to TCS added to unfilled PDMS (Figure 2). Addition of TCS to composites based on NI.3TC and C30B also affects the dispersion state of the platelets. In the former case the position (3.45°) of the (001) is reflection is the same both in NI.3TC powder and in the composite (Figure 4(b-i+ii)), therefore indicating a significant

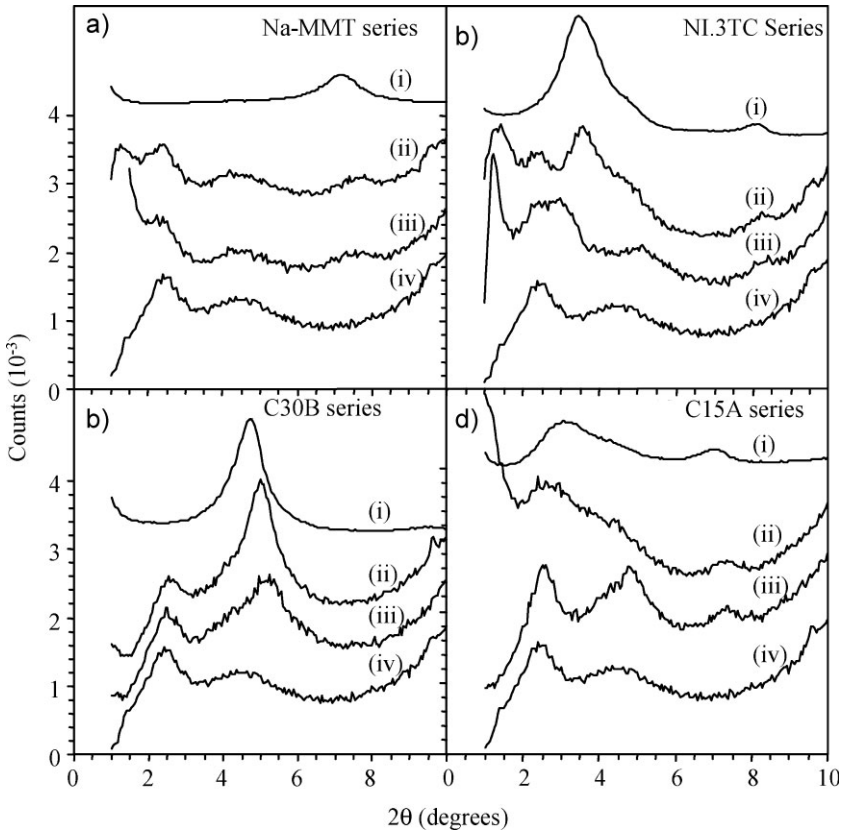

Figure 4.
WAXS data for (a) CNa^{+}, (b) NI.3TC, (c) C30B and (d) C15A based composites, containing 5 wt% MMT silicate. Pattern designations as follows: (i) MMT/o-MMT powder (count scale divided by 10), (ii) composite without TCS (1.8 wt%), (iii) composite with TCS and (iv) unfilled PDMS. Note intensities of composites have been normalised to the amorphous halo reflection peak of unfilled PDMS.

fraction of the NI.3TC is not intercalated by PDMS. However, a hint of a reflection at 1.45° (interlayer spacing 5.13 nm) is also present in the PDMS/NI.3TC composite and could relate to a fraction of the NI.3TC being intercalated by PDMS to spacing that may correspond to an expanded double vertical monolayer of octadecyl (chains which could easily accommodate TCS when it is added). Addition of TCS to the NI.3TC based composite however, leads to a shift of the reflection at 3.45° (interlayer spacing 1.63 nm) to about 3° (interlayer spacing 1.98 nm) (Figure 3b (iii)), and the broad reflection at 1.45° appears to have become more intense. This data certainly assists in the explanation of the relatively good controlled release of TCS in the NI.3TC based composite despite TCS having only weak interaction with NI.3TC in the FMC cell. What little interaction that does occur in the FMC may be with the edge hydroxyl groups of the o-MMT platelets. Blockage of the latter sites has been known [7] to ease polymer intercalation due to entry of chains into the gallery being less hindered.

In the case of C30B based composites (Figure 4(c)) the intensity of the C30B (001) reflection has reduced on addition of TCS therefore indicating enhanced PDMS intercalation. Development of a reflection corresponding to higher interlayer spacing is not apparent (or outside the measurement range of the WAXS system used)

though its appearance may be obscured by the inherent reflection in the unfilled PDMS at 2.5° (Figure 4(c-iv)). A small amount of C30B platelet exfoliation may have occurred and could explain the sustained release effect observed. Increased intercalation/exfoliation resulting from TCS addition may be related adsorption of TCS on the edge hydroxyl groups as discussed previously. It is interesting to note that C30B resulted in the greatest enhancement of M_{50}, an observation that supports exfoliation as proposed above. The relatively low surfactant content of C30B will also ensure that there will be a large portion of uncoated silicate surface to enable favourable interaction with the PDMS chains thereby affording relatively good filler-matrix adhesion over the strain range encountered during stiffness measurement. The relatively large reduction in stiffness observed on addition of TCS supports reduced filler-matrix interaction due to displacement of PDMS chains on exposed areas of silicate platelets by TCS.

Composites based on C15A (Figure 4(d)) gave the most interesting (and somewhat unexpected) WAXS data. Firstly the WAXS data for the C15A powder (Figure 4(d-i)) must be considered as it reflects rather non-uniform intercalation of the surfactant and even indicates presence of a small fraction of unmodified MMT (reflection at 7°). Well controlled incorporation of ditallow dimethylammonium at the level specified to be in C15A usually results in a uniform layer structure that is characterised by narrow reflection peaks and higher order reflections up to (or even beyond) the fourth order.[8] In contrast, C15A has a very broad (001) reflection peak giving an average interlayer spacing of 1.93 nm. The breadth and low intensity of the reflection peak is due to a high level of stacking disorder combined with a relatively small number of platelets per tactoid. The former effect is related to the platelets within tactoids not being spaced in a parallel fashion, due to non-uniform adsorption of the surfactant, and the latter effect may be due to mechanical break-down of tactoids during micronisation. Within the PDMS based composite (without TCS) a significant fraction of the C15A may have had an interlayer spacing that was outside the measurement range of the WAXS system used; the increase in counts below 2° may be due to the base of a reflection peak. The reflection at ca. 2.5° (coincident with the inherent reflection from the unfilled PDMS) may correspond to platelets separated by fully extended, but slightly slanted, hydrogenated tallow alkyl chains in an arrangement that is proposed by Százdi and Pukánszky.[9] Addition of TCS to PDMS/C15A leads to a disappearance of the suspected reflection peak below 2° and an increase in the sharpness of the reflection at 2.5° (interlayer spacing 2.44 nm), together with the appearance of new reflection at 4.75° (interlayer spacing 0.90 nm). This apparent increase in geometric uniformity (even relative to the C15A powder) hints at the possibility of TCS giving rise to a pinning effect that prevents an increase in interlayer spacing beyond 2.44 nm. The molar heat of adsorption of TCS on C15A (Figure 1(b)) suggests a significant hydrogen bonding contribution that could be explained by the diagram shown in Figure 5(a), the latter shows that the TCS can be accommodated within the arrangement of tallow alkyl chains proposed by Százdi and Pukánszky. The hydrogen bonding interactions between the TCS and aminyl nitrogen of the surfactant together with interaction between the adjacent TCS molecules may serve to glue the platelets together and so prevent further expansion. The reflection corresponding to an interlayer spacing of 0.90 nm may be assignable to a bi-layer of surfactant as sketched in Figure 5(b). The latter arrangement will also be able to accommodate TCS though it is suspected that the Százdi-Pukánszky arrangement is responsible for the majority of the controlled release effect observed.

In order to attempt to increase the limiting leached concentration of TCS to a level just beyond the MIC of *C. Albicans*, a

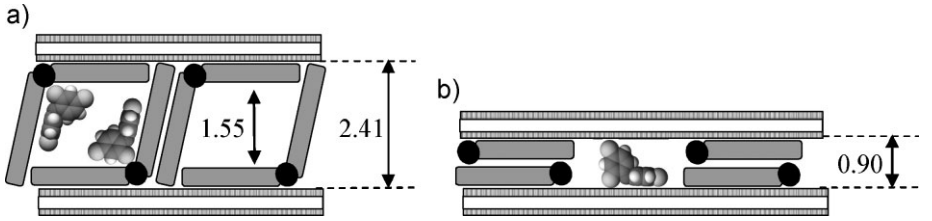

Figure 5.
Diagrams showing possible accommodation of TCS within C15A featuring; (a) the Százdi and Pukánszky arrangement of alkyl chains, and (b) a horizontal bi-layer with both alkyl chains in contact with the MMT platelet surface. All dimensions in nm.

formulation based on 20 wt% C15A and 4 wt % TCS was prepared. The WAXS data is shown in Figure 6 and shows a strong narrow (001) reflection peak at 2.5° (d-spacing 3.68 nm, interlayer spacing (ILS) 2.44 nm) with progressively less intense reflections corresponding to d-spacings of 1.86 nm and 1.24 nm.

The latter two peaks are likely to be due to higher order reflections and are a manifestation of uniform ordering of platelets that can be accommodated by the Százdi-Pukánszky arrangement of C18 alkyl chains. Interestingly, the TCS release characteristics, were virtually identical the composite containing 3 wt% TCS (Figure 7), an observation that supports the encapsulation mechanism proposed in which leaching of TCS is controlled by desorption from rhomboid profile tube-like spaces (pores) formed by self-assembled C18 alkyl chains of the intercalant.

Conclusion

Aspects influencing the release of TCS from composites based on o-MMT and PDMS have been explored. The major conclusions drawn from this work are as follows: Predictions concerning controlled release characteristics associated with layered substrates cannot always be related to the adsorption behaviour of the active from solution; interactions between the host polymer and the layered substrate must also be taken into account. In the case of NI.3TC, C30B and even CNa+, controlled release of TCS was observed, despite there being relatively small interaction of the TCS from heptane. WAXS of the composites indicated enhanced intercalation and possible fractional exfoliation of the latter MMT platelets on addition of TCS. Further work is required to resolve the mechanism though it is likely to relate

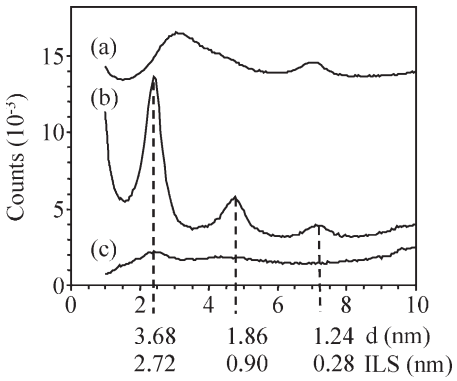

Figure 6.
WAXS patterns of (a) C15A, (b) PDMS containing 15 wt% C15A, 4 wt% TCS and (c) unfilled PDMS.

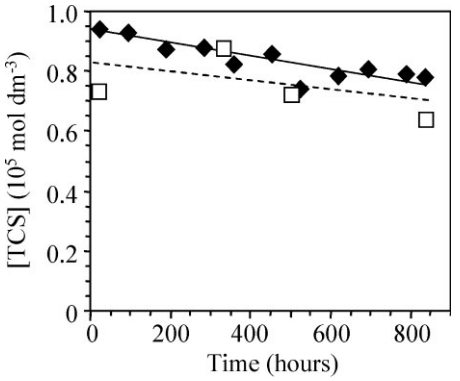

Figure 7.
Effect of TCS/C15A level on release characteristics; (3 wt% TCS/15 wt% C15A, □ 4 wt% TCS/15 wt% C15A.

to possible blockage of edge hydroxyl groups combined with adsorption of TCS on the now-exposed basal surfaces.

In terms of its strong TCS adsorption activity in the FMC together with the most sustained TCS release into water from a PDMS based composite, C15A arguably afforded the most predictable behaviour of the o- MMTs examined. WAXS data however hinted at some interesting effects relating to accommodation of TCS within pores formed in the gallery spaces by self-assembled alkyl tails of the intercalant.

Acknowledgements: M. Al-Mansoor, T. Abdallah, A. Langfield and P. Skingle of MMU for preparation and examination of the composites.

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