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Thio-urethanes Improve Properties of Dual-cured Composite Cements

APPENDIX

MATERIALS AND METHODS

Thio-urethane Synthesis

Appendix Figure 1 shows the chemical structures of the starting materials, as well as a cartoon of the resulting thio-urethane network. The ratio of 1:2 isocyanate:thiol was determined based on the Flory-Stockmeyer gelation theory (Odian, 2004). That way, gelation is avoided during synthesis of the crosslinked oligomer, and pendant thiol functionalities are available to undergo chain transfer reactions with the vinyl on the secondary matrix.

Microtensile Bond Strength Test

Microtensile bond strength was tested with 36 caries-free human third molars extracted for periodontal reasons (Institutional Ethics Committee, approval 040/2013). Teeth were stored in 0.5% chloramine at 4ºC and used no longer than 1 mo after extraction. Deep dentin (the most critical for adhesion) was exposed by removing the cusps 2.0 mm above the CEJ, then wet polished with a 600-grit SiC paper (CarbiMet 2; Buehler, Lake Bluff, USA) for 30 sec. An etch-and-rinse adhesive (Adper Singlebond 2; 3M ESPE) was applied according to manufacturer instructions. Indirect composite (Z250, 3M ESPE, A2, built in a silicone mold cured in a TRIAD oven for 5 min, Dentsply) or a glass ceramic (IPS Empress, Ivoclar Vivadent, HT-A2) was used to fabricate blocks (8 × 5 × 3 mm), wet polished with 600-grit SiC paper for 30 sec and sonicated. The ceramic surface was then etched with hydrofluoric acid (10%) for 60 sec; the composite surface was cleaned with phosphoric acid (37%) for 1 min, both followed by 1 min of silane application. The blocks were cemented with the commercial cement (control and modified groups), under 2 Kg of load applied for 60 sec, then light cured for 60 sec with a LED lamp (700 mW/cm²) on each side of the composite/ceramic block. Only the commercial material was used in this test to minimize the number of human teeth needed for the study, per Institutional Ethics Committee instructions. Samples (*n* = 6) were stored for 1 wk in distilled water (37ºC) before being sectioned into ~1-mm² matchsticks. The sticks were glued to a testing fixture and then tested in tension in a universal testing machine at 0.5 mm/min. Each tooth produced 8-12 sticks, whose results were grouped by tooth. After statistical power analysis, *n* = 6 was shown to be sufficient for an overall confidence level of 95%. Appendix Table 1 shows the number of specimens obtained per tooth for each material, as well as the number of premature failures. Because the number of failures was less than 4% and homogeneously distributed among the groups, those specimens were not considered for the statistical analysis, which therefore only included surviving specimens. Results within each cement material group were analyzed by 1-way analysis of variance and Tukey's test for multiple comparisons (α = 0.05). The failure patterns were evaluated by stereomicroscopy/scanning electron microscope.
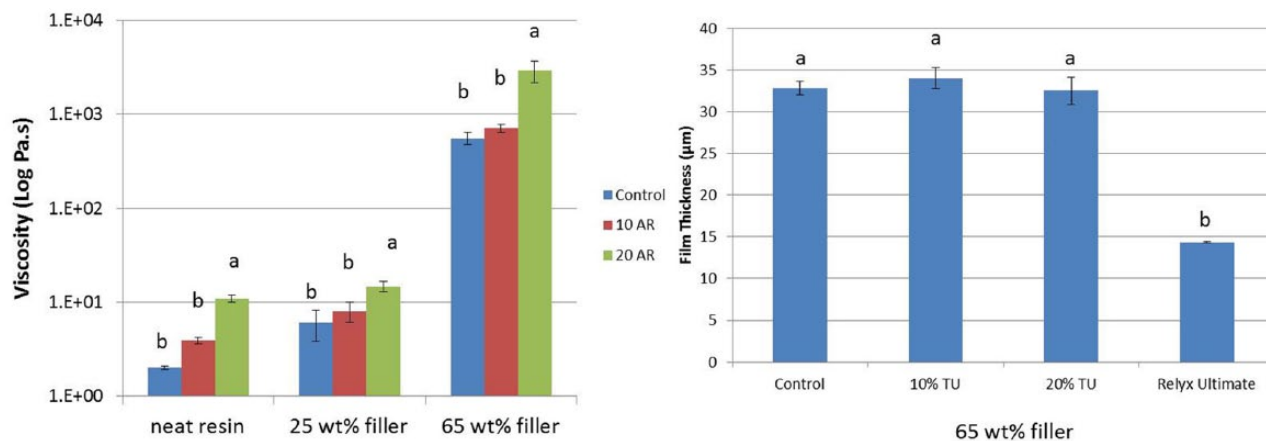
Viscosity Measurements

Viscosity (*n* = 3) was measured in a cone-plate rheometer (ARES, TA Instruments, New Castle, DE, USA). Approximately 1 g of each material was placed between 20-mm diameter plates and tested at 1 Hz with a gap of 0.3 mm.

Film Thickness

Film thickness (*n* = 3) was determined according to ISO 4049 (International Organization for Standardization, 2000); 200 mg of freshly mixed cement was sandwiched between mylar sheets (50 × 50 mm). A 150-N load was applied to an area of 200 mm² for 300 sec. The material was photoactivated for 60 sec using the LED light source used in the previous experiments (BluePhase 2, 700 mW/cm²). The film of cement was peeled off the mylar sheet and measured with a digital caliper to 0.001 mm.

Degree of Conversion of Specimens Cured through a Composite/Ceramic Disc

The irradiance affects reaction kinetics and final degree of conversion (Lovell *et al.*, 2001). Since the proposed materials are routinely photoactivated through indirect restorations, with a significantly reduced light intensity, a second set of experiments

Appendix Figure 1. Starting materials and reaction scheme for the synthesis of thio-urethane oligomers.

Appendix Table 1. Average Number of Stick Specimens per Tooth for Each Experimental Group and Percentage Premature Failure

Indirect Material: Cement Type	Specimens Obtained per Tooth (n = 6)	Percentage Premature Failure[a]
Composite		
Control	14.4 ± 3.4	2.8
10 AR	16.6 ± 4.2	3.2
20 AR	14.8 ± 0.8	2.6
Ceramic		
Control	14.7 ± 0.5	1.1
10 AR	14.3 ± 1.4	1.2
20 AR	15.3 ± 2.6	1.1

[a]Dentin/material debonding during the 24-hr storage period between cutting and microtensile bond strength testing.

verified the degree of conversion of thio-urethane modified cements photo-activated through a 2-mm-thick (10 mm in diameter) specimen of both IPS Empress (A2) and Z250 composite (A2). Cement specimens, irradiation conditions, and conversion measurements were otherwise described in the main text.

RESULTS AND DISCUSSION

Viscosity and Film Thickness

Appendix Figure 2 shows results of viscosity in logarithmic scale for the experimental materials (control and modified by the addition of 10 or 20 wt% thiourethane). For every material, the addition of the highest thio-urethane concentration led to increased viscosity in relation to the control, within each inorganic filler loading level. However, the filler composition played a much greater role in viscosity than did the addition of the thio-urethane alone. It is important to note that, in spite of the greater viscosity, the addition of thio-urethane oligomers did not affect the film thickness of the experimental material, for either concentration (p = .423), in the conditions tested. The commercial control presented statistically lower film thickness (19 ± 2 μm) than the experimental control (26 ± 1 μm). All materials tested presented film thickness within the standard recommendation for clinical use (<50 μm) (ISO 4049; International Organization for Standardization, 2000).

Appendix Figure 2. Viscosity for the experimental materials with 0, 25, and 65 wt% filler loading. Film thickness was measured only for the 65 wt% filler loading and the commercial control. Same superscripts within the same filler loading indicate statistical similarity for each test (α = 5%).

Appendix Table 2. Degree of Conversion of 65 wt% Filler Materials Measured in Specimens Photoactivated through a Mylar Strip (Directly), a Composite Disc, or a Ceramic Disc

	Directly		Composite Disc		Ceramic Disc	
	Immediate	After 72 hr	Immediate	After 72 hr	Immediate	After 72 hr
Control	62.3 ± 2.3[b]	74.4 ± 3.2[a]	44.2 ± 0.9[a]	53.7 ± 5.9[a]	41.8 ± 3.4[a]	51.5 ± 6.7[a]
10 wt% TU	69.1 ± 0.8[a]	73.9 ± 0.5[a]	44.8 ± 1.4[a]	58.1 ± 1.5[a]	42.9 ± 1.8[a]	54.1 ± 5.4[a]
20 wt% TU	58.3 ± 1.2[b]	70.8 ± 0.5[a]	23.0 ± 7.7[b]	36.1 ± 4.5[b]	32.3 ± 3.6[b]	50.1 ± 5.8[a]

Values in mean ± SD. Measurements were taken immediately after photoactivation and after 72 hr of dry storage in dark containers. Values followed by the same superscript are statistically similar (α = 5%).

## Degree of Conversion for the 65 wt% Filler Loading

In this second set of experiments, the 65 wt% filler materials were photoactivated either through a mylar strip ("directly", 700 mW/cm^2 actually reaching the specimen) or through discs of composite or ceramic (280 or 350 mW/cm^2, respectively, actually reaching the specimen) to simulate clinical conditions. The results of conversion obtained after photoactivation through the mylar strip were similar for the 25 wt% filler loading (as described on the main document) and for the 65 wt% filler loading. In summary, regardless of the filler concentration, conversion values measured immediately after photoactivation through the mylar decreased for the highest thio-urethane concentration in comparison to the control (Appendix Table 2), but all materials reached similar conversions after 72 hr. When the materials were photoactivated simulating composite or ceramic crown cementation conditions, the overall values of degree of conversion were lower, as expected, based on the lower irradiance caused by light attenuation through the prosthetic material. However, at least for the ceramic disc, the materials modified with thio-urethanes reached conversion similar to the control after 72 hr of storage, in spite of the decreased irradiance. Future studies will concentrate on a more systematic variation of irradiance and its influence on the degree of conversion of thio-urethane-modified materials.

## Mechanical Properties in Flexure of 65 wt% Filler Materials

The materials formulated with 65 wt% filler were also tested in 3-point bending using the method described on the main manuscript. The results in Appendix Figure 3 show the same trends presented by the commercial material modified by the addition of thio-urethanes (Table 2). In summary, for the 65 wt% filler materials, the flexural strength and modulus were not statistically different from the control (p = .179 and .442, respectively), whereas the toughness increased significantly for the 20% TU material in relation to the unmodified control (p = .030). Similarly to the 25 wt% material, this can be explained by the increased flexibility imparted to the network by the thio-urethane bonds, which has been demonstrated to increase the energy necessary for crack propagation in those materials (Li *et al.*, 2009).

Polymerization Stress Test

Appendix Figure 4 shows the stress × time curves for the (a) experimental and (b) commercial materials at 25 and 65 wt% inorganic filler loadings. The rates of stress development were lower for the thio-urethane modified materials, as could be anticipated based on the likely delay in gelation/vitrification
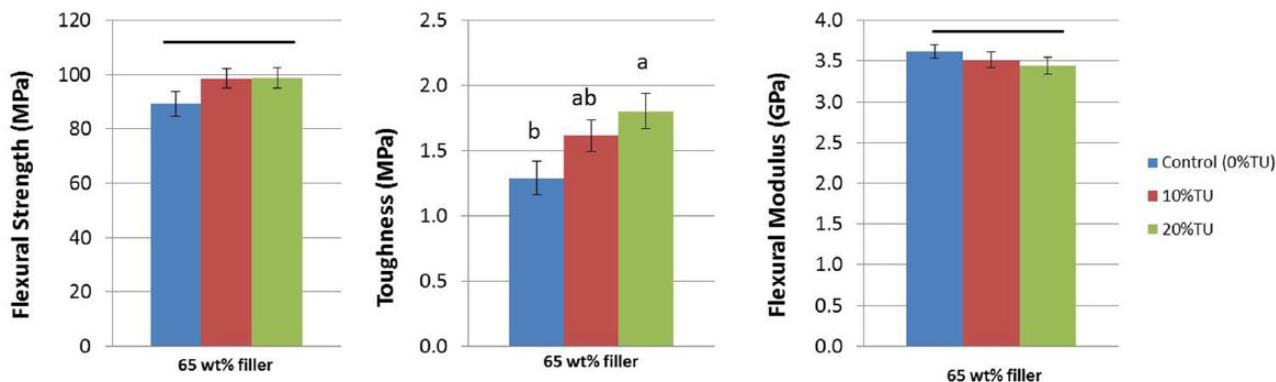
Appendix Figure 3. Mechanical properties in flexure assessed for the 65 wt% filler materials. Horizontal bars indicate statistical similarity. Values followed by the same superscript are statistically similar (α = 5%).
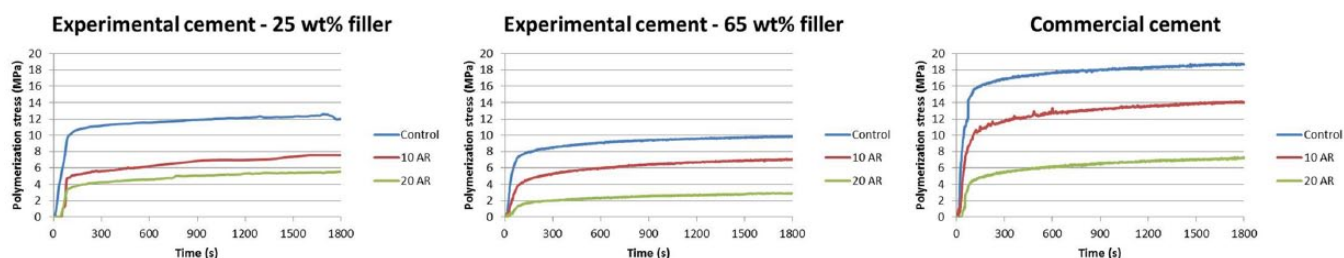
Appendix Figure 4. Real-time polymerization stress for the (**a**) experimental materials with 25 and 65 wt% filler loading and for the (**b**) commercial materials.

reported for thiol/vinyl-based materials (Pfeifer *et al.*, 2011). It needs to be pointed out, however, that this is strictly speculative. Due to the dual-cure nature of the cements tested here, it is not possible to accurately measure kinetics of conversion (unless an initiator of the iniferter type is used; Zhang *et al.*, 2013), so the delay in gelation/vitrification, though very likely, could not be verified. Moreover, the thio-urethane oligomers also likely influence the rate of modulus development during polymerization, which in turn also influences the rate of stress development. Therefore, rather than delving into the very complex interaction among the factors governing stress development, this study focused on the practical and verifiable effect of the addition of thio-urethane oligomers, which was to effectively reduce the overall stress achieved by methacrylate networks. Indeed, for both filler loadings and for the commercial materials, the stress reduction with the addition of thiourethane was significant, ranging from 30% to 70%, as detailed in the results section of the main document. The stress reduction obtained with the 65 wt% filler loading was greater than the reduction observed for the 25 wt% filler counterparts, at least in part likely because of the expected reduction in shrinkage achieved at higher filler loadings. In addition, for the more highly filled material, a slight, though not statistically significant, decrease in modulus was observed for the 20 wt% thio-urethane compared to the control, as opposed to the increase in modulus observed for the same groups with 25 wt% filler. In other words, for the more highly filled material, the addition of thio-urethane had an even greater impact in stress reduction without compromise to conversion, accompanied by a significant increase in toughness and only a slight decrease in modulus.

APPENDIX REFERENCES

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