Fibre-reinforced injectable orthopedic composites with improved toughness and cell compatibility

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Statement of Purpose: Vertebral fractures result in severe back pain and immobility but can be stabilized by PMMA cement (e.g. Simplex-P®) injection. Inherent drawbacks with PMMA, however, include irreproducibility (hand mixing). Moreover, small monomer or activator (e.g.DMPT) leaching and high heat generation can kill cells and shrinkage causes loosening[1]. Recent clinical studies show the advantages of using composite bone cement (e.g.Cortoss®) instead of PMMA for vertebroplasty[2]. Use of dimethacrylates in Cortoss, instead of less cell compatible methyl-methacrylate (in PMMA) is of particular benefit. Furthermore, with dimethacrylates, conversion need only be 50% for monomers to potentially all be bound. Cortoss, however, exhibits lower strength with no toughness (brittle fracture)[3] and is therefore less able to absorb energy before breaking. Although of less concern than with PMMA, Cortoss still produces significant heat and shrinkage upon set[4]. The aim of this study was to compare properties of novel composites containing lower shrinkage diluent monomer (PPGDMA), polymerisable activator (NTGGMA) and fibres with Cortoss® and Simplex®.

Methods: Base monomer, with different diluents and activators (Table 1), was combined with initiator, glass fillers and fibres. Curing profiles were assessed through FTIR. Biaxial flexural strength (BFS) and toughness were determined. Biocompatibility of extracts was assessed through MTS Assay (MG-63 cell, ISO 10993-12:2012).

Serial no.	Diluent Monomers	Activator
F1	PPG-DMA	NTG-DMA
F2	TEG-DMA	NTG-DMA
F3	TEG-DMA	DMPT
C	Cortoss®	DMPT
S	Simplex®	DMPT

Table 1: Formulations

Results & Discussion: The working times of all experimental formulations were comparable with Cortoss. Working times for composites can be much shorter than for Simplex as they are supplied premixed in syringe form. Subsequent setting time (Half-life) was shorter for F1 and F2 than Cortoss or Simplex. This reduces possibility of monomer leaking from the site of application in vivo (Figure 1 and Table 2).

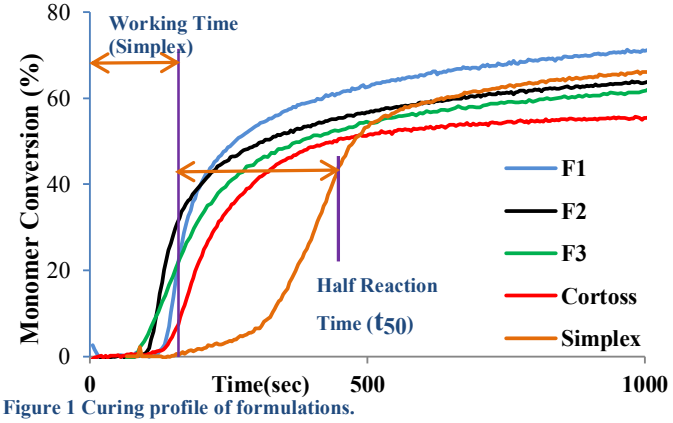

Figure 1 Curing profile of formulations.

[Arrows indicate Simplex working and half reaction time (t_{50})].

The final conversion was higher for all experimental formulations (74-80%) than for Cortoss (Table 2). This reduces subsequent potential monomer leaching. The heat generation and shrinkage of the experimental formulations were also beneficially lower than with commercial materials. Furthermore, the strength and toughness of F1 and F2 were higher than F3 or either commercial material.

No.	*Half life (t_{50}) (s)* 95%-CI	*Final conversion (%)* 95%-CI	*Heat (cal/cc)* 95%-CI	*Shrinkage % (vol/vol)* 95%-CI	*Flexural strength (MPa)* 95%-CI	*Fracture toughnes (Mj/m^3)* 95%-CI
F1	*80* ±5	79.3 ±0.2	22.9 ±0.3	3.7 ±0.02	170 ±5	32 ±1
F2	*86* ±7	76.2 ±0.5	26.4 ±0.3	4.3 ±0.02	184 ±5	28 ±2
F3	*133* ±5	74.1 ±0.2	25.7 ±0.3	4.2 ±0.02	143 ±4	24 ±2
C	130 ±5	64 ±0.5	30.1 ±0.3	5.0 ±0.02	99 ±4	7 ±1
S	362 ±17	81 ±0.2	46.8 ±0.3	7.6 ±0.02	128 ±4	22 ±3

Table 2: Half-life, final conversion, heat generation and mechanical properties of experimental formulations and commercial products

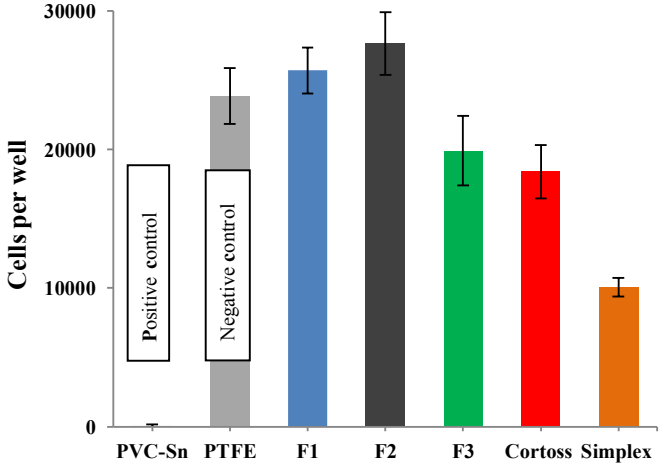

Figure 2: Biocompatibility of Formulation.

Extracts from F3, Cortoss and Simplex all caused a reduction in cell proliferation (Figure 2). This is likely due to release of both DMPT and monomers. With Simplex in particular, release of mono-methyl-methacrylate with poor cell compatibility is likely to have occurred (Figure 2).

Conclusions: Experimental formulations F1 and F2 are fast setting and have high conversion but low heat generation and shrinkage. They also have high strength and toughness and good cell compatibility when compared to Cortoss® and Simplex®.

References:

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