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Modifying dental composites to formulate novel methacrylate-based bone cements with improved polymerisation kinetics, and mechanical properties

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ABSTRACT

Objectives: The aim was to develop bone composites with similar working times, faster polymerisation and higher final conversion in comparison to Cortoss™. Additionally, low shrinkage/heat generation and improved short and longer-term mechanical properties are desirable.

Methods: Four urethane dimethacrylate based composites were prepared using tri-ethylene-glycol dimethacrylate (TEGDMA) or polypropylene dimethacrylate (PPGDMA) diluent and 0 or 20 wt% fibres in the glass filler particles. FTIR was used to determine reaction kinetics, final degrees of conversions, and polymerisation shrinkage/heat generation at 37 °C. Biaxial flexural strength, Young's modulus and compressive strength were evaluated after 1 or 30 days in water.

Results: Experimental materials all had similar inhibition times to Cortoss™ (140 s) but subsequent maximum polymerisation rate was more than doubled. Average experimental composite final conversion (76%) was higher than that of Cortoss™ (58%) but with less heat generation and shrinkage. Replacement of TEGDMA by PPGDMA gave higher polymerisation rates and conversions while reducing shrinkage. Early and aged flexural strengths of Cortoss™ were 93 and 45 MPa respectively. Corresponding compressive strengths were 164 and 99 MPa. Early and lagged experimental composite flexural strengths were 164–186 and 240–274 MPa whilst compressive strengths were 240–274 MPa and 226–261 MPa. Young's modulus for Cortoss™ was 3.3 and 2.2 GPa at 1 day and 1 month. Experimental material values were 3.4–4.8 and 3.0–4.1 GPa, respectively. PPGDMA and fibres marginally reduced strength but caused greater reduction in modulus. Fibres also made the composites quasi-ductile instead of brittle.

Significance: The improved setting and higher strengths of the experimental materials compared to Cortoss™, could reduce monomer leakage from the injection site and material fracture, respectively. Lowering modulus may reduce stress shielding whilst quasi-ductile properties may improve fracture tolerance. The modified dental composites could therefore be a promising approach for future bone cements.

1. Introduction

Orthopedic reconstruction procedures involving bone defects, atrophy, osteoporotic fractures, traumatic injuries, or bone resection due to tumors may require reparative surgery with bone substitutes [1,2]. When preferred biological grafts are not an option, the use of bone cements may be deemed necessary. These materials are considered a common and viable approach in a variety of procedures. Applications include vertebroplasty, kyphoplasty, arthroplasty or in the surgical correction of defects in the maxillofacial region [1,3–5]. Currently, the most widely used materials for this are polymeric acrylic bone cements

generally composed of poly(methyl) methacrylate (PMMA) or calcium phosphate bone cements [3,6,7].

PMMA cements can be easily molded and have a working time that may be partially controlled by varying temperature. Major drawbacks, however, have been identified [8]. Problems include significant polymerisation shrinkage reducing potential bone integration. Furthermore, there is often slow, or incomplete final, monomer conversion. These issues can allow monomer leaching from the site of application, or reduce mechanical strength, respectively [9,10]. Additionally, the biocompatibility of PMMA cements is further questionable since the setting reaction is exothermic. Heat generation is proportional to

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polymerisation shrinkage. Both are high due to low molecular weight monomers having a high concentration of polymerising groups. Raising the temperature of the biomaterial in situ is greatly undesirable and may lead to damage of the surrounding tissues. In fact, polymeric bone substitutes have been linked to cases of bone necrosis and bone cement implantation syndrome [5,11]. Finally, PMMA does not have osteoconductive properties [12].

To address the above issues, modifications to PMMA matrices and/or the addition of novel components has been undertaken [3,12]. One family of newer bone cements are resin-based composites. Light activated composites have been used in restorative dentistry since the 1970s but were more recently modified for bone applications [3,13]. Bone composites need to be “chemically”, instead of light cured. This occurs upon mixing of 2 pastes containing an initiator and activator. Cortoss™ (Orthovita, Malvern, PA, USA) is a popular commercial choice. It is composed of Bisphenol-A diglycidyl dimethacrylate (Bis-GMA) and Bisphenol-A dimethacrylate ethoxylated (Bis-EMA) with triethylene glycol dimethacrylate (TEGDMA) as the organic matrix. This is filled with combeite and silicon dioxide [6]. Despite its claimed bioactivity through apatite precipitation, this has not been observed in vitro. Cortoss also shows inferior monomer conversion values and strength, compared to experimental competitors [14].

Conventional dental composites are composed of an organic matrix containing hydrophobic and viscous high molecular weight base monomers such as Bis-GMA or urethane dimethacrylate (UDMA). Inclusion of lower molecular weight TEGDMA to improve flow characteristics, however, increases polymerisation shrinkage and heat generation [15]. As a substitute, poly(propylene) glycol dimethacrylate (PPGDMA) has been employed. PPGDMA can raise conversion but simultaneously reduce shrinkage due to its molecular weight being two-fold higher than that of TEGDMA [16]. Panpisit et al. (2019) have previously formulated UDMA/PPGDMA bone composites with reactive calcium and strontium phosphate fillers. The study found that PPGDMA could improve paste stability and reaction kinetics, while also compensating for polymerisation shrinkage in comparison to TEGDMA systems. The authors concluded that these formulations may be promising for bone applications due to water sorption induced release of ions that promote apatite precipitation. Flexural strengths of both these formulations and Cortoss, however, were all less than half that of a commercial PMMA cement [17].

Dental composites are quasi-brittle in nature whilst PMMA is quasi-plastic. Additionally, when placed, composites can have an initially high strength, but may be plasticized by water sorption upon aging. This plasticisation leads to a decline in flexural strength and increased fracture risk. It also, however, may beneficially reduce modulus. Too high modulus can cause stress shielding which, through reduction in loading of adjacent bone, may lead to bone resorption [18]. One method of controlling composite mechanical properties has been through addition of silane-coated glass-fibres [19–21]. Fibres could theoretically make composites quasi-plastic and extend the elongation before final break.

The aim of this study is therefore to assess the impact of adding PPGDMA as a replacement for TEGDMA, on the reaction kinetics and mechanical properties of modified dental composites for bone repair. Simultaneously, the effect of glass fibres is determined. The first null hypotheses of the present study is that the experimental formulations and Cortoss do not have significantly different:

- (1) polymerisation reaction kinetics (including inhibition time, half-life, reaction rate and final degree of conversion)
- (2) polymerisation shrinkage and heat generation or
- (3) mechanical properties (including early versus later time biaxial flexural strength, Young’s modulus, compressive strength and brittle versus pseudo-plastic behaviour).

The second and third null hypotheses are that replacing TEGDMA by PPGDMA or 20 wt% of the glass filler particles by glass fibres has no

significant effect on the same properties.

2. Materials and methods

2.1. Materials

Monomers urethane dimethacrylate (UDMA; Product code: 100112), TEGDMA (Product code: 100102) and 2-hydroxyethyl methacrylate (HEMA; Product code: 100220) were obtained from DMG Dental-Material Gesellschaft mbH (Hamburg, Germany). PPGDMA was from Polysciences (Product code: 04380–250; Warrington, USA). The polymerisation initiator benzoyl peroxide came from Sigma Aldrich (Product code: 15205BH; Gillingham, UK) while the activator Na-N-tolyl-glycine glycidyl methacrylate (NTGGMA) was obtained from Esschem (Product code: 133736–31–9; UK).

Silanized barium-boroaluminosilicate glass fillers (7 µm average particle size) were from DMG Dental-Material Gesellschaft mbH (Product code: 680326). Silane coated borosilicate glass fibres, with a mean size of 15×300 µm (aspect ratio: 20), were purchased from MO-Sci (Product code: 0322201-S; Rolla, Missouri, USA). Cortoss™ (Orthovita Malvern, PA, USA), was available as two pastes in double-barrel syringes with automatic mixing tips.

2.2. Preparation of experimental formulations

An analytical balance (AG 205 Mettler Toledo, UK) was used to weigh all monomers and fillers during preparation. Composite monomer phase was prepared by mixing 70 wt% UDMA with 25 wt% TEGDMA or PPGDMA, as a diluent monomer. 5 wt% HEMA was also added as a co-solvent to improve handling properties and flow. Monomers were mixed using a magnetic stirrer until clear (~15 min at 300 rpm), then stored in amber glass jars at 4°C until required. Separate initiator and activator liquids were prepared by adding either BP (1 wt%) or NTGGMA (0.75 wt%) respectively.

The composite filler phase consisted of barium aluminosilicate glass filler particles with or without fibres (0 or 20 wt%). Experimental formulations and respective codes are shown in Table 1. The filler phase was mixed with the initiator and activator liquid monomers at a 3:1 powder-to-liquid ratio using a centrifugal mixer (SpeedMixer DAC 140.0 FVZ, 2000 rpm, 60 s; Synergy Ltd., High Wycombe, UK). The resultant initiator and activator pastes were packed into double barrel syringes (Sulzer Chemtech, UK). These keep the activator and initiator paste separate until required. Upon mixing with the syringe mixing tips,

Table 1

Experimental formulations, their respective abbreviations, monomers and glass fibre content and Cortoss composition.

Code	Base monomer, Initiator and Activator (wt% of final monomer phase)	Diluent monomer (wt% of monomer)	Glass fibre (wt% of filler)
T	UDMA (70)	TEGDMA (25)	0
TF	UDMA (70)	TEGDMA (25)	20
P	Benzoyl Peroxide (0.5)	PPGDMA (25)	0
PF	NTGGMA (0.375)	PPGDMA (25)	20
Cortoss™	Organic matrix Bisphenol-A-glycidyl dimethacrylate (Bis-GMA), bisphenol-A-ethoxy dimethacrylate (Bis-EMA), TEGDMA, benzoyl peroxide (BP) and dihydroxyethyl-p-toluidine (DHPT)		Fillers Boroaluminosilicate glass, silica particles, combeite glass-ceramic particles

initiator and activator concentrations were 0.5 and 0.375 wt% of the monomer, respectively. These levels were selected as they provided formulations with similar times between initial mixing and before any polymerisation to that of Cortoss.

2.3. Reaction kinetics

For determination of reaction kinetics, Fourier-Transform Infra-Red (FTIR) spectra were obtained at 37 °C using an FTIR spectrometer (Perkin-Elmer 2000, Perkin-Elmer, Buckinghamshire, UK). This was coupled with a temperature-controlled, golden gate, diamond, attenuated-total-reflection (ATR) accessory. To confine the samples, a metal mold ($\varnothing = 10$ mm, $h = 1$ mm) was placed around the ATR diamond crystal. Samples were subsequently dispensed from the double barrel syringe, through their automatic mixing tips, into the metal mold. Acetate sheet was placed on the top surface of the dispensed material to remove the possibility of an oxygen-inhibition layer. FTIR spectra of the lower surface were obtained every 4 s for 45 min, at a resolution of 4 cm^{-1} (TimeBase, Perkin-Elmer, UK). Spectral wavenumber acquisition ranged from 1200 to 1800 cm^{-1} .

Fractional degree of monomer conversion (D_c), inhibition time (t_i), reaction half-life ($t_{0.5}$) and polymerisation rate (R_p) were calculated using the 1319 cm^{-1} ($\nu[\text{C-O}]$) stretch peak [22]. D_c was calculated using Equation (1):

$$D_c = (h_0 - h_t)/h_0.$$

h_0 and h_t were taken as peak absorbance at 1319 cm^{-1} wavenumber, above background at 1352 cm^{-1} initially and at time t after the start of the mixing. Final degree of conversion ($D_{c,\text{max}}$) was obtained by linear extrapolation of late time D_c values versus inverse time to zero (as inverse of zero is infinity). This fraction was converted to a percentage by multiplying by 100. t_i and $t_{0.5}$ were calculated as described in Panpisut et al. (2019) from reaction extent (ξ) given by Equation (2):

$$\xi = \frac{D_c}{D_{c,\text{max}}}.$$

Inhibition time is the time polymerisation begins after mixing whilst $t_{0.5}$ is the time when reaction extent is 0.5. The rate of polymerisation, R_p was calculated from the gradient of D_c versus time, using sets of 3 time points. The maximum rate ($R_{p,\text{max}}$), observed immediately following the inhibition time, is reported.

2.4. Theoretical polymerisation shrinkage and heat generation

To calculate polymerisation shrinkage and heat generation, it was assumed that one mole of polymerising carbon-carbon double bonds in methacrylates, produces 57 kJ of heat and volumetric shrinkage of 23 cm^3 [23]. The number of moles of reacted double bonds per unit volume, can then be calculated using Equation (3):

$$N(\text{mol}/\text{cm}^3) = D_c \cdot \rho \left(\sum \frac{n_i x_i}{M_w} \right).$$

Σ indicates a sum over all the monomers present in the liquid phase. For each monomer, M_w is molecular weight (g/mol), n_i number of double bonds per molecule and x_i their mass fraction in the composite. Composite density, ρ (g/cm^3) was calculated, assuming an ideal mixture of fillers and monomers and no volume changes occurring due to voids formation, using Equation (4):

$$\frac{1}{\rho} = \frac{x}{\rho_m} + \frac{1-x}{\rho_f}.$$

ρ_f and ρ_m are the densities of the filler and monomer mixture, respectively. x , is the total monomer weight fraction (0.25) in the composite. Polymerisation shrinkage as a percentage is then estimated using Equation (5):

$$V(\%) = 100k \cdot N,$$

where k is 23 cm^3 . The heat generation is then $V/100$ multiplied by 57 $\text{kJ}/23 \text{ cm}^3$.

2.5. Mechanical properties

Biaxial flexural strength (S) and Young's modulus (E) of the specimens were evaluated using ball-on-ring method. Disc-shaped specimens were made using metal brass rings (1 mm thickness; 10 mm internal diameter), covered top and bottom with an acetate sheet and allowed to cure for 24 h. Discs were stored in 10 mL of distilled water and were incubated at 37 °C either for 24 h or for a period of 1 month. At each time point, 8 discs were used for each formulation to determine the strength and modulus ($n = 8$). Each disc was placed on a knife edge ring support (4 mm radius) and then loaded by a spherical tip using a 10 kN Instron cell (Instron 4503 Universal testing machine, Norwood, MA, USA), at a cross head speed of 1 mm/min.

To calculate strength Equation (6) was used [24]:

$$S = F/t^2 \{ (1 + \nu)[0.485 \ln(a/t) + 0.52] + 0.48 \}$$

where F represents the load being applied when the material fails (in N), t is the specimen thickness, a is the radius of the support ring and ν is the Poisson ratio (0.3).

Modulus was calculated using Equation (7):

$$E = (\Delta J/\Delta W_c) \times (\beta_c \cdot a^2/r^3)$$

$(\Delta J/\Delta W_c)$ is the gradient of force versus the displacement curve, β_c is the center deflection function (0.5024).

For compressive strength (C), specimens were made using stainless steel split ring moulds, with an internal diameter and height of 4×6 mm, respectively. After mixing, each material was pressed into their respective moulds and immediately covered with an acetate sheet. All discs were allowed to set for 24 h before testing. After removal from moulds, samples were polished around the edges using 1200 grit silicon carbide paper and a polishing machine (Struers Labopol 5; Struers Ltd., Solihull, West Midlands, UK). Compressive strength was determined using a protocol in ISO-5833 for acrylic bone cements. After each incubation period (24 h or 1 month at 37°C), cylinders ($n = 8$) were compression tested on the Instron, using a load cell of 50 kN and crosshead speed of 1 mm/min. The following equation (8) was used for compressive strength:

$$C = P/\pi r^2,$$

where P is the maximum load (kN) and r is the radius of the specimen.

2.6. Statistical analysis

To analyse data, Statistical Package for the Social Sciences v.27 for Mac (SPSS, IBM Corporation, Armonk, NY, USA) was used. For reaction kinetics, data parametric assumptions were met. Factorial ANOVA design was therefore used to assess the influence of changing (1) monomer content and (2) fibre content, followed by Tukey's HSD for post-hoc. Games-Howell was used when data were heteroscedastic ($D_{c,\text{max}}$). All inferential statistics tests were conducted at a set significance level of 5%.

3. Results

3.1. Reaction kinetics

Fig. 1 provides example data of reaction extent versus time normalized by $t_{0.5}$ observed with PPGDMA compared with TEGDMA-containing composites. These show how t_i and $t_{0.5}$ are defined. The

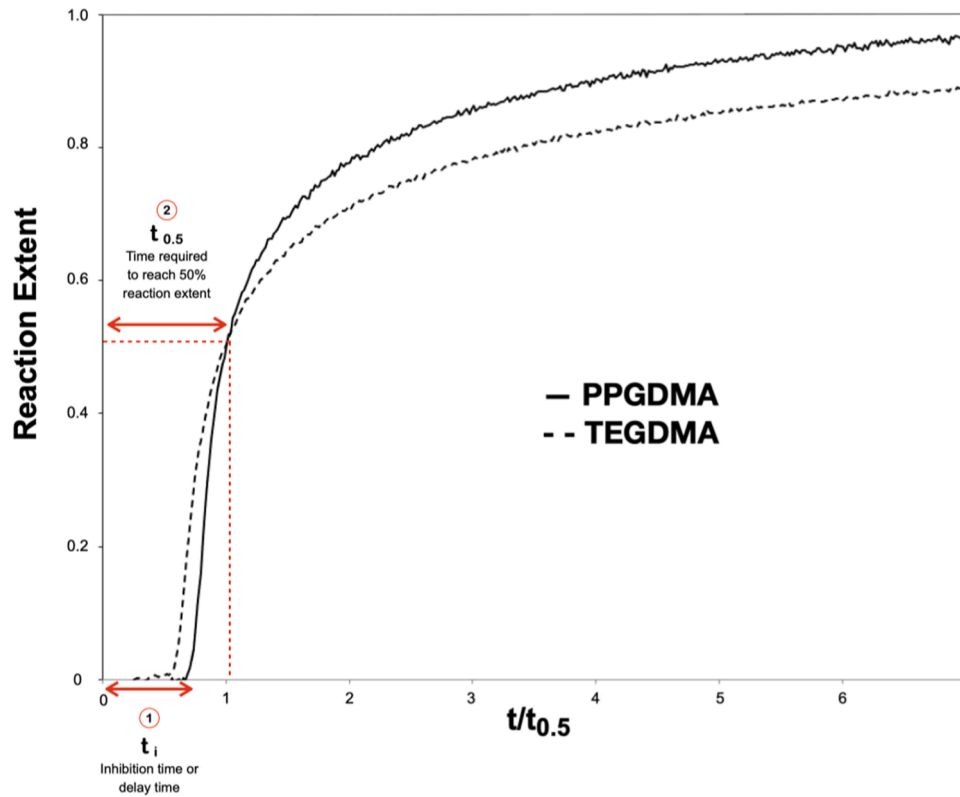


Fig. 1. Example normalized data of reaction extent versus time (t) divided by the half-life ($t_{0.5}$) for T and P formulations. For P, the difference between the inhibition time (t_i) and $t_{0.5}$ is smaller and reaction extent reaches 1 more quickly than for T indicating sharper set.

shorter time interval between the inhibition time and half-life combined with reaction extent approaching 1 more rapidly indicates sharper set with the PPGDMA formulations.

3.1.1. Inhibition time and half-life

Average inhibition times and half-lives are provided in Fig. 2. The average inhibition time for the experimental formulations was comparable with that of Cortoss. Results for PPGDMA formulations, however, were slightly higher than for TEGDMA-containing samples. Factorial ANOVA confirmed the type of monomer had a significant impact

($p < 0.001$), while inclusion of fibres did not ($p = 0.06$).

As for half-life, Cortoss™ revealed statistically significantly higher mean half-life compared to all other groups (Tukey's HSD, $p < 0.001$) indicating less sharp set. Factorial ANOVA reported that changing from TEGDMA to PPGDMA ($p = 0.039$) and addition of fibres ($p = 0.003$) caused only a small increase in $t_{0.5}$.

3.1.2. Reaction rate and D_C

Maximum reaction rates and degrees of conversion are provided in

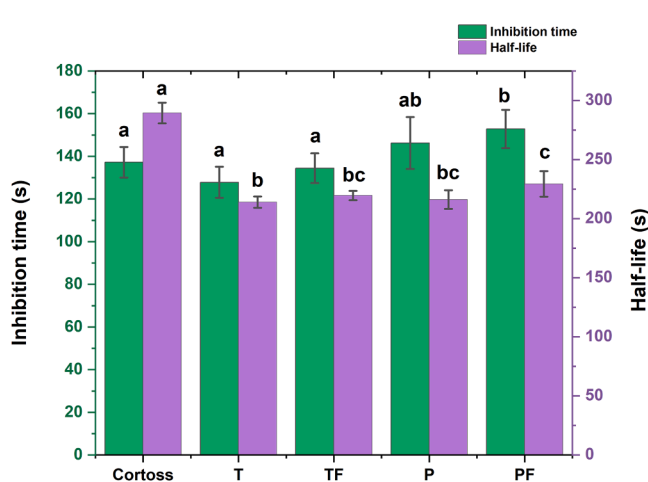


Fig. 2. Inhibition time and half-life ($n = 3$). Error bars represent 95% confidence intervals. Statistical difference can be read only between bars with the same color, where, common letters between bars indicate non-significant differences, and different letters indicate statistically significant differences (Tukey's HSD, $p < 0.05$).

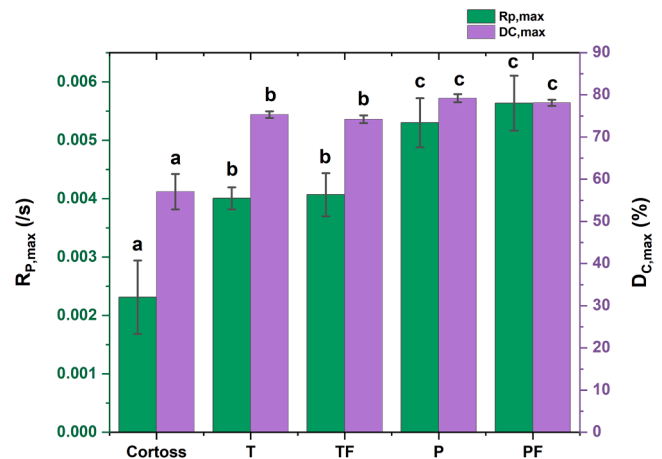


Fig. 3. Maximum rate of polymerisation ($R_{p,max}$) and final extrapolated degree of conversion ($D_{C,max}$) ($n = 3$). Statistical difference can be read only between bars with the same color, where, common letters between bars indicate non-significant differences, and different letters indicate statistically significant differences (Tukey's HSD, $p < 0.05$, in exception to D_C , which was compared using Games-Howell post-hoc).

Fig. 3. Reaction rates were significantly higher for PPGDMA systems compared to TEGDMA formulations (factorial ANOVA, $p < 0.001$) consistent with sharper set. Cortoss™ had a slower and inferior reaction rate than all experimental formulations (Fig. 3). The same trend was seen with $D_{C,max}$ (%). Again, the most significant factor was the type of monomer used, since formulations with PPGDMA achieved higher D_C (ANOVA, $p < 0.001$; $\eta^2 = 0.9$). For this property, Cortoss™ (57%) was again significantly lower than all other formulations (T – 75, TF – 74; P – 79 and PF – 78%) (Games-Howell, $p < 0.001$).

3.1.3. Polymerisation shrinkage and heat generation

A bar chart containing volumetric shrinkage (vol%) means and 95% confidence intervals, is provided in Fig. 4. The second y axis is shifted to enable the same bar to simultaneously provide heat generation as it is proportional to calculated shrinkage. Polymerisation shrinkage of experimental formulations was found to be between 3.1 (P) and 3.6 vol% (TF), while Cortoss™ was comparable (3.4 ± 0.1 vol%). The inclusion of glass fibres did not affect shrinkage or heat generation (ANOVA, $p > 0.05$). These properties did, however, decrease slightly when the diluent monomer was changed from TEGDMA to PPGDMA.

3.1.4. Mechanical properties

Cortoss and P and T composites exhibited quasi-brittle fracture and a sharp drop in stress at strain values of ~ 0.14 mm (Fig. 5a). Conversely, formulations with fibres (TF and PF) exhibited quasi-plastic behaviour (Fig. 5b). With TF and PF constant stress was observed from strain of 0.1–0.2 and 0.15–0.3 respectively (Fig. 5b).

Means and 95% CI for flexural strength, elastic modulus and compressive strength are provided in Fig. 6. Cortoss™ flexural strengths dropped by half from 93 ± 7 at 24 h to 45 ± 4 after 1 month aging. Values for all experimental formulations were much higher irrespective of time (Tukey's HSD $p < 0.001$). They ranged from 149 (P at 1 month) to 186 MPa (T at 24 h). Increased aging, using PPGDMA instead of TEGDMA and adding fibres all caused a small but experimentally significant reduction in flexural strength (factorial repeated measures ANOVA, all at $p < 0.001$).

Cortoss™ had a flexural modulus which ranged between 3.3 ± 0.2 at 24 h to 2.2 GPa at 1-month (Tukey's HSD $p < 0.001$). Experimental formulations at a given time point all had higher modulus. As with flexural strength, increased aging time, TEGDMA replacement by PPGDMA and addition of fibres caused a significant decline in modulus (factorial repeated measures $p < 0.001$). The levels of effect on modulus, however, were greater than the effects on strength. An interaction effect was also noted between the impact of the variable time and the inclusion

of fibres ($p < 0.001$).

Similarly, all experimental formulations had a much higher compressive strength than Cortoss at 1 day and 1 month ($p < 0.001$). Factorial analysis showed that increased time, use of PPGDMA and adding fibres all caused a small but experimentally significant decline (factorial repeated measures ANOVA, both at $p < 0.001$).

4. Discussion

4.1. Experimental material composition

In this investigation, UDMA was selected as the base monomer for the experimental composites. UDMA is increasingly being used in dental composites and adhesives as a replacement for Bis-GMA. It provides various potential benefits including improvements in flow, polymerisation and strength [25,26]. TEGDMA was used as it is present in Cortoss™ and is a popular diluent monomer in a wide range of dental composites. PPGDMA has only recently been employed in a commercial dental material but shows promise in comparison with TEGDMA [16, 26]. The initiator, BP is a standard component in PMMA bone cements. The amine activator NTGGMA, however, is a non-conventional choice. It was selected due to it providing much sharper set compared to identical formulations with more standard amine containing systems and gave a higher degree of final monomer conversion [27]. Furthermore, NTGGMA is a tertiary aromatic amine with a methacrylate group attached that may co-polymerise with other methacrylates [28]. This reduces the chance of cytotoxic issues that are a known problem with other activators [29,30]. The glass filler is a standard dental composite component, but the fibres are nonstandard. As with the glass particles, the fibres that were added were also silane treated to form a bond with the monomer phase, crucial to achieving high strength. Fibres level was fixed at 20% as higher levels provided similar pseudo-plastic behavior and extension at final break. The choice of fibres with an aspect ratio of 20 can be justified by aiming for a balanced improvement in flexural strength and modulus while maintaining flowability, which aligns with the objective of this study. This intermediate AR value falls within the range of ARs tested in previous studies which confirmed these balanced properties [31], making it a reasonable choice.

This study found significant and large differences between the experimental and commercial composites' kinetic and mechanical properties. Changing the diluent monomer from TEGDMA to PPGDMA and partial replacement of filler particles by fibres also had significant, although generally much smaller effects on these properties so kinetic and mechanical property null hypotheses can be rejected. Despite higher conversions the experimental formulations had on average similar calculated shrinkage and heat generation to that of Cortoss. Replacement of TEGDMA by PPGDMA, however, significantly reduced shrinkage so further null hypotheses can be rejected.

4.2. Reaction kinetics

Polymerisation kinetics are particularly important in the case of bone cements as they affect how materials can be placed and final material properties. For example, the inhibition time for the composites indicates the working time that the clinician has between mixing and injection. For this study, the levels of initiator and activator included in the experimental materials were selected so that comparable working times were obtained to that of Cortoss™. Required working times for composites are shorter than for PMMA, because two pastes are easier/quicker to mix than the PMMA powder and liquid. A short interval between the inhibition time and half-life corresponds with a fast reaction rate. Rapid reaction is required to reduce potential for leakage from the site of application. Final polymerisation extent is tightly linked to material mechanical behaviour and potential longer-term toxicity associated with uncured monomer leaching [32,33]. Factors influencing reaction kinetics include initiator chemistry, initiator/activator levels,

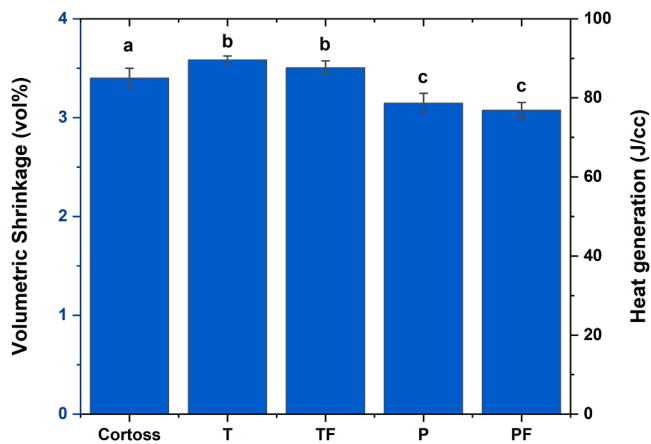


Fig. 4. Volumetric shrinkage (vol%) and heat generation (in J/cc) mean values ($n = 3$) with 95% CI are shown. Different small letters indicate statistically significant differences (Tukey's HSD, $p < 0.05$). Systems containing PPGDMA as a diluent monomer show less volumetric shrinkage and heat generation.

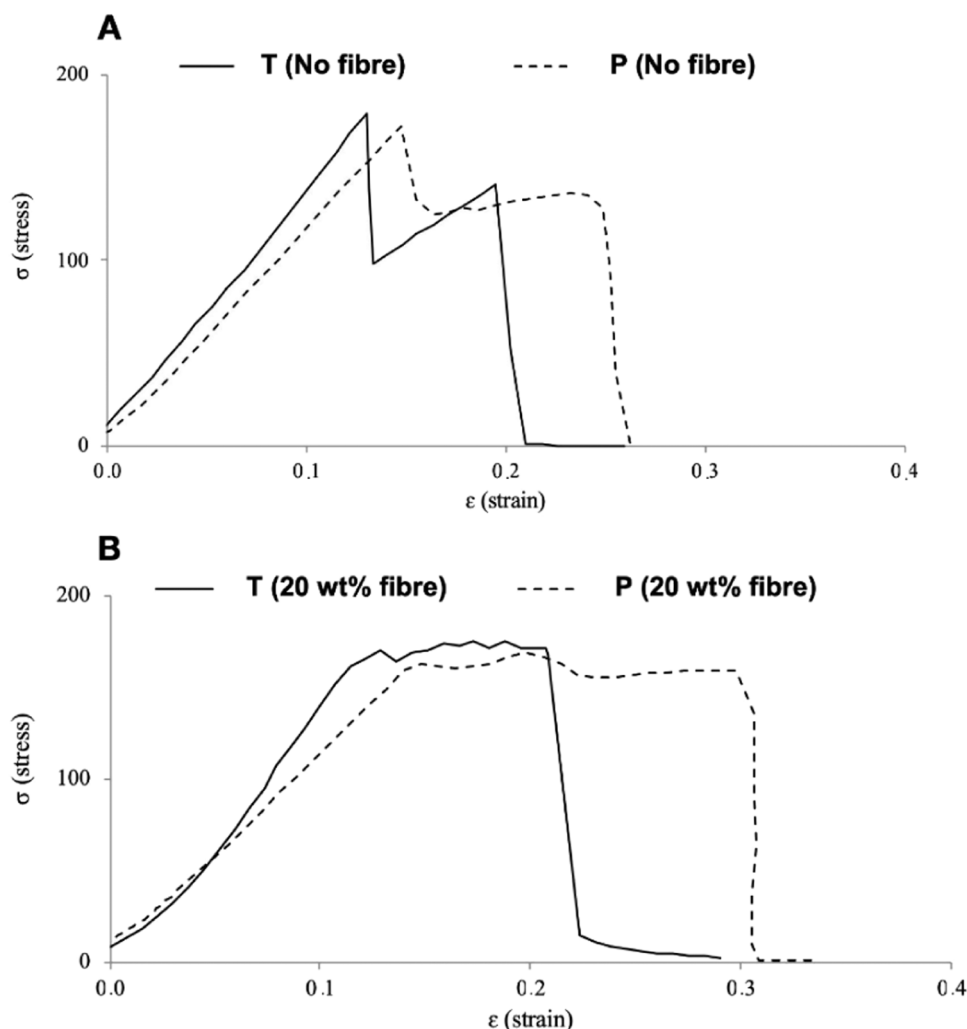


Fig. 5. Representative stress strain plots for experimental formulations (a) With no fibre containing formulations quasi-brittle fracture is observed. (b) Quasi-ductile behaviour is found with fibre reinforced formulations.

inhibitor concentration, monomer chemistry, temperature, or oxygen permeability [14,26]. In this work, the ATR unit was set at 37°C to mimic body temperature.

Inhibition time, half-life, reaction rate and final conversions observed in this study for Cortoss were all slightly lower than expected from previous work [15]. A possible explanation is a combination of different assessment temperatures, batches and / or paste aging times. Previous work has shown inhibition times can increase whilst final conversions decrease with composite paste aging. This problem can be reduced with UDMA-based formulations upon TEGDMA replacement by PPGDMA [15].

In previous studies, formulations with UDMA/PPGDMA had average inhibition times of 85 s, whilst those with UDMA/TEGDMA were just 24 s at room temperature [15]. These would be expected to be less than half these values at body temperature, and far too low to provide viable commercial formulations. Assuming stationary state polymerisation kinetics, the inhibition time is expected to be inversely proportional to the initiator and activator concentrations [27]. The longer inhibition times in the above new work were therefore achieved through more than halving the initiator and activator concentrations.

Following the inhibition period, polymerisation rapidly accelerates. Maximum rates for the experimental materials were comparable with previous work using similar monomer systems but higher initiator and activator concentrations [15]. From kinetic theories, rates are expected to be proportional to the square root of initiator and activator

concentrations [27]. It is probable that similarities in rates are due to the earlier work being undertaken at room instead of body temperature which counterbalances the higher initiator levels.

With PMMA, 100% final conversion is required to ensure all monomers are bound to slower moving polymer chains. With dimethacrylate-containing composites, however, conversion occurs upon monomers joining polymer chains and upon a slower crosslinking reaction. If the crosslinking process is very much slower, all monomers may be bound to a polymer chain at ~50% conversion. With the experimental materials this could occur between 1½ - 2 min after the inhibition time. With Cortoss™ it is expected at ~ 3½ min after the inhibition time. Potential time for leakage of the experimental materials from the site of application is therefore likely reduced compared with the commercial material Cortoss™.

The $D_{C,max}$ seen in the commercial control, Cortoss™ is low in comparison with the UDMA-based formulations, because it is a Bis-GMA-based system. This monomer is less flexible and has a higher glass transition temperature (T_g), limiting conversion levels [34]. Furthermore, UDMA/PPGDMA-based polymers systems, these are known to achieve high conversion levels when compared to UDMA/TEGDMA mixtures [14,16,26]. The longer chain in PPGDMA separating the two methacrylate groups, is more flexible than TEGDMA, in turn enabling greater crosslinking. Additionally fast reaction with the PPGDMA groups, may cause greater localized temperature rise due to a shorter time for heat dissipation, and thereby higher final conversion.

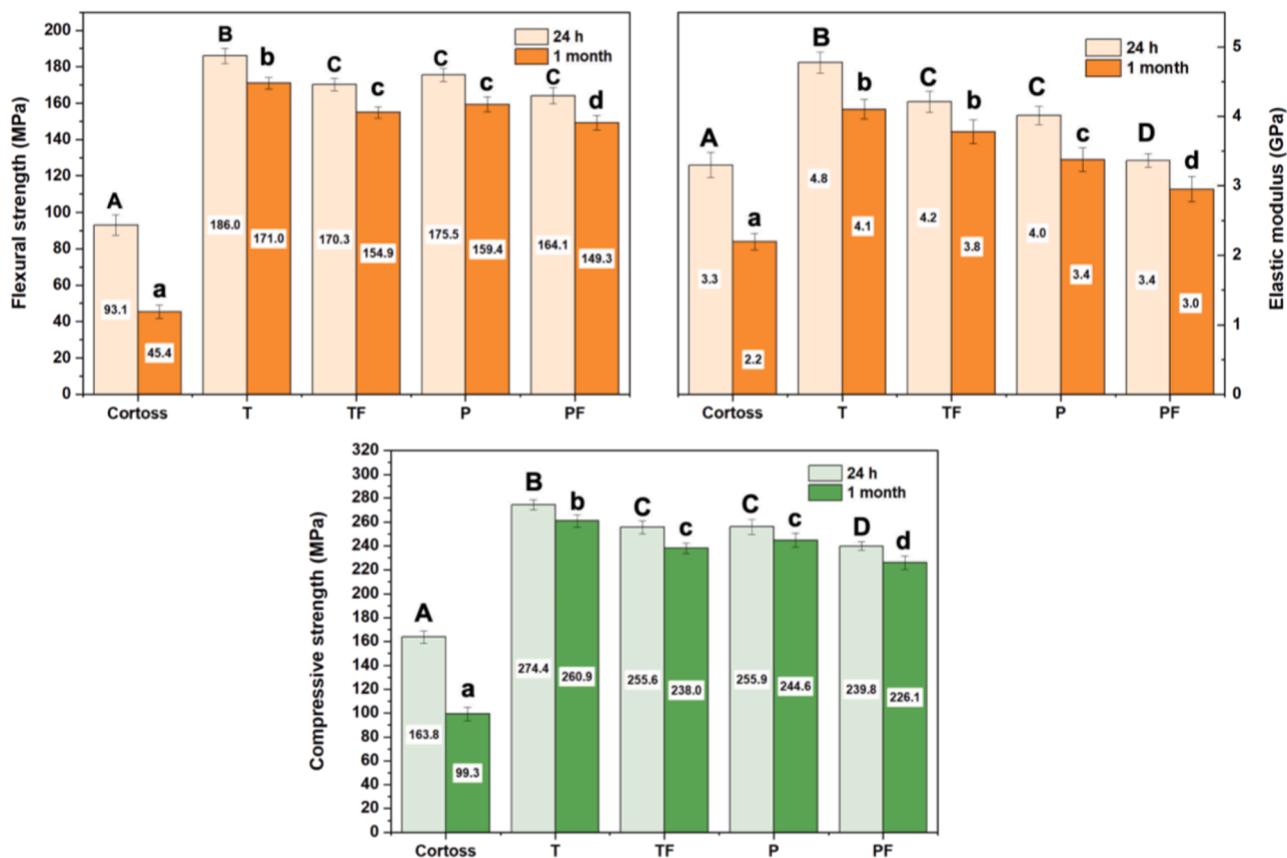


Fig. 6. Mechanical properties (flexural strength, elastic modulus and compressive strength) at two distinct time points – 24 h and 1 month aging in water ($n = 8$). Mean values and 95% CI are shown. Cortoss™ shows weaker flexural and compressive strength compared to experimentals and less elastic modulus (Tukey's HSD, $p < 0.05$). Also, a marked reduction of the mechanical properties was seen with Cortoss over time compared to that experienced by experimental formulations (Tukey's HSD, $p < 0.001$). Different capital letters show statistical differences between 24 h bars, while small letters are used to measure differences between 1 month data. Regarding 24 h vs 1 month, if 95% CI do not overlap, they are significantly different.

The methodology can be explained by previous work, that has shown that the height of the peak per methacrylate group at 1319 cm^{-1} gives less variability with monomer type than the 1640 cm^{-1} C=C peak [22]. This latter has commonly been used to assess composite conversion. Furthermore, the 1319 cm^{-1} peak has double the absorbance thereby improving accuracy of monomer conversion determination. When used to determine monomer conversion in commercial composites its use was proven to give reduced variability. The above previous work also confirmed that normalisation of data using a peak that was unchanging during polymerisation is unnecessary, if composites are cured directly on the ATR-FTIR diamond, as in this work.

4.3. Polymerisation shrinkage and heat generation

Polymerisation shrinkage is related to the molecular weight of monomers, the number of double bonds in each methacrylate monomer and its molecular weight and the final monomer conversion reached [24]. The experimental materials that were formulated had lower monomer content (25 wt%) compared with Cortoss™ (32 wt%). This compensates for higher experimental material conversion. Additionally, using the higher molecular weight diluent PPGDMA monomer enabled further lowering of volumetric shrinkage [35]. Heat generation is theoretically proportional to shrinkage. The average values of heat of polymerisation obtained for Cortoss™ determined through differential scanning calorimetry (DSC) were 45, 63 and 55 J/g at 25, 30 and 40° C, respectively [36]. Dividing the above calculated heat generation by Cortoss™ density, gives a heat generation of 55 J/g. This is in good agreement with the previous DSC data at 40° C. This is despite

assumptions in calculations that heat generation per mole of reacted groups is equal to the average value for methyl methacrylate and does not vary with conversion or crosslinking level. Cortoss™ has shown a mean temperature variation, after placement, lower than that of PMMA cements, but higher than composites in a previous study [37]. Whilst PPGDMA-systems generated less amount of heat overall, compared to the TEGDMA systems, the heat output was faster due to their sharper set. This may translate into a higher temperature, but for a shorter period. This temperature may be below the critical threshold of bone and is not expected to be damaging as the blood circulation and poor thermal conductivity of the material may allow a cooling effect [38].

4.4. Mechanical properties

The mechanical properties of the composites with no fibres observed in this work are similar to those obtained previously, but with light instead of chemical activated polymerisation. In the previous studies it was shown that strength and modulus declined in the first week and this correlated with water sorption [24]. As water sorption was tending to equilibrium between 1 week and 1-month, further changes in mechanical properties during this period were found to be small. One month of sample storage was therefore selected for mechanical property assessment in this new work, in addition to the 24-hour point already required by the standard ISO 4049 test.

The DC_{max} has a significant influence on the mechanical properties of the resulting polymers [26,39]. As the concentration of plasticising monomers in a polymerising matrix declines, the glass transition temperature (T_g) increases. When this approaches the temperature of the

surroundings, the matrix will change from a rubber to glass. This is associated with a sharp decline in polymerisation rate and increase in modulus and strength [40]. As stated earlier, UDMA has a lower T_g than Bis-GMA. The experimental materials are therefore able to reach higher conversion values, as longer time is required for the glass transition temperature of the composite matrices to reach that of the surroundings. Also, in higher D_C levels, there is more crosslinking resulting in a dense and stiff polymer network, translating into higher modulus values [34].

If the composite matrix phase absorbs water this may inevitably re-plasticise the matrix, reducing T_g , strength and modulus [41,42]. In all experimental formulations, there was a slight decline in mechanical properties with time, after immersion in water. This was not comparable to the higher decline seen with Cortoss™. Continuing long-term polymerisation in the glassy state within UDMA-based dental resins was shown to lead to higher T_g [40]. As polymerisation also continued in this study for the experimental composites, it might have helped to reduce long-term plasticising effects of water-sorption. However, this decline was still much higher for Cortoss™, which may be attributed to weak filler-matrix interactions and water sorption phenomena that can cause filler failures and filler-matrix debonding [43]. Insufficient filler-matrix bonding is responsible for initial reduced flexural strengths and fracture toughness.

For Cortoss™, final monomer conversions observed above are similar to those of commercial dental composites, but the early strengths much lower [24]. This, combined with the considerable further lowering of strength with time may restrict material use to lower load-bearing applications. The flexural strength observed after 1 month in this study (45 MPa) is slightly lower than observed previously (58 MPa) [15]. The difference could be a consequence of lower conversion rates. Low values, in comparison with dental composites, however, is more likely due to poor bonding between the matrix and fillers. Poorer filler bonding would additionally explain the much lower strengths of UDMA-based composites seen in earlier work, compared with these new experimental formulations [15]. Addition of hydrophilic particles to the previous formulation [15], were likely responsible for water sorption and decreased long-term strength. These, unlike the particles and fibres in the present study, were not silanized. Moreover, the amine activator, NTGGMA, is a monomeric surfactant which might improve the wetting and interaction of the filler phase with the polymeric phase leading to higher strength [44].

An ideal material for bone substitution would have high strength but low elastic modulus [45]. This would make it able to withstand a higher strain before breaking. This stress shielding mechanism can prevent adjacent bone fractures, specifically important in vertebral surgery. The elastic modulus of the material is dependent on the modulus and volume fraction of each phase of the composite [46]. In addition to this, the level of porosity of the paste also influences the elastic modulus [47]. A strong proportional correlation has been reported between the filler load and respective modulus of the material, which can also explain the higher modulus of the experimental materials [48]. Cortoss has a 69 wt% (41 vol%) filler load, while the experimentals are 75 wt% (~50 vol%), explaining the modulus values. Overall, The T formulation was the strongest and stiffest out of all materials. The PF formulation, however, provides a compromise through having good strengths whilst maintaining a lower modulus to reduce potential stress shielding. The above findings also showed that PPGDMA formulations have slightly lower modulus compared to TEGDMA-based formulations. This may be a consequence of the high ratio of more flexible PPGDMA. This is beneficial since these formulations were able to maintain higher strength while lowering the modulus. In fact, comparing Cortoss™ to PPGDMA-systems, the elastic modulus was found to be similar, whilst the strength is much lower in Cortoss™. The strain at break may thus be similar. The compressive strengths were less sensitive than flexural to changes in formulation and aging. With PPGDMA it was possible to obtain formulations with high strength, without large percentage increase in modulus. A high modulus is the effect of the filler particle

composition of composites, but also of good matrix-filler interactions and low water sorption [26].

It was hypothesized that adding glass fibres to the experimental composites could increase its strength and give an interesting mechanical behaviour. However, the type of fibres used, their size and critical concentration all play a role in determining the mechanical properties. Literature shows conflicting effects of fibre on composite strength. Some studies showed that fibre incorporation in a small volume fraction can improve the flexural strength of composites [49–51], whereas other studies show they may act as a stress point, that can serve as crack initiation sites, resulting in a decrease in flexural strength [52]. The main purpose of fibre is to hinder or control the crack propagation by fibre deformation, fibre pulling and fibre bridging [53,54]. Fibres have been verified to prevent brittle fracture, by holding the formulation in place even after fracture. Fibre addition in this study slightly decreased the strength of the composites. This could be due to the agglomeration of the fibres [55], or possibly less effective silane coupling. A pseudo-plastic behaviour is able to withstand higher load without fracture, absorbing more energy in the plastic deformation phase than the preceding elastic deformation [56]. This combines the ability of a brittle, high strength material but with higher values of elongation. Instead of failing due to a brittle fracture, materials may undergo plastic deformation [57].

5. Conclusion

New composites were developed, with comparable working time to Cortoss™ but with advantageous reaction kinetics, such as a sharper set, high conversion levels, while still achieving reduced shrinkage and heat generation. UDMA/PPGDMA systems, in replacement of TEGDMA, significantly improved reaction rates and conversion levels. Mechanical properties (flexural strength, modulus, and compressive strength) at 1 month aging were much higher for experimentals than for the commercial control Cortoss™. Bone composites showed overall better polymerisation and mechanical properties than the commercial control. Modifying dental composites made from dimethacrylate monomers, with an improved chemical-cure system containing NTGGMA, seems to be a promising approach for future bone cements.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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