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Structure-Property Relationships in Quaternary Ammonium Urethane-Dimethacrylate Copolymers: The Effect of the Diisocyanate Core

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Grzegorz Chladek: Methodology; Investigation; Formal analysis; Data curation. **Anna Mertas:** Methodology; Investigation; Formal analysis; Data curation.

Abstract

This study investigates how structural modifications in quaternary ammonium urethane-dimethacrylates (QAUDMAs) affect the physicochemical, mechanical, and biological properties of QAUDMA-containing dimethacrylate copolymers. Specifically, it examines variations in the diisocyanate (DI) core: tetramethylxylene diisocyanate (TMXDI), isophorone diisocyanate (IPDI), dicyclohexylmethane-4,4'-diisocyanate (CHMDI), and diphenylmethane-4,4'-diisocyanate (MDI), as well as the N-alkyl substituent: octyl (QA8) and decyl (QA10). Experimental copolymers were prepared by replacing urethane dimethacrylate (UDMA, 40 wt.%) with QAUDMA in a conventional dental resin system, while retaining bisphenol A-glycidyl methacrylate (Bis-GMA) 40 wt.% and triethylene glycol dimethacrylate (TEGDMA) 20 wt.%. Monomer formulations (40(QAUDMA)_m) were evaluated for viscosity (η), density (d_m), and refractive index (RI). Copolymers (40(QAUDMA)_p) were assessed for density (d_p), degree of conversion (DC), polymerization shrinkage (S), glass transition temperature (T_g), flexural strength (FS), modulus (E), hardness (HB), *in vitro* antibacterial activity against *Streptococcus mutans*, and cytocompatibility using L929 fibroblasts. Monomer mixtures usually retained their physicochemical characteristics, except η , which exhibited higher values than the reference. Copolymers showed improved physicochemical characteristics, while maintaining clinically relevant mechanical performance. Importantly, all 40(QAUDMA)_ps completely prevented bacterial adhesion to the material surface, while maintaining acceptable cytocompatibility, with cell viability above 70% for most formulations. Among the tested systems, TMXDI-based copolymers demonstrated the most balanced overall performance. These results indicate that controlling the DI core structure provides a rational strategy for designing QAUDMA-based resin matrices with tailored antibacterial, mechanical, and biological properties. The obtained structure-property relationships offer valuable insights for the development of functional resin matrices for future dental composite materials.

Keywords: dental resins; quaternary ammonium urethane-dimethacrylates; antibacterial polymers; physical properties; mechanical properties; cytocompatibility

1. Introduction

Contemporary restorative dentistry recognizes dental caries as a multifactorial, biofilm-mediated disease. Therefore, restorative treatment is only one component of comprehensive caries management, together with biofilm control, dietary modification, and fluoride exposure. Conventional dental composite restorative materials (DCRMs) act as passive mechanical replacements and neither eliminate the bacterial cause of caries nor prevent biofilm accumulation at the tooth–restoration interface [1]. As a result, secondary caries remains a leading cause of restoration failure [2]. This is mainly due to the accumulation of cariogenic biofilm, particularly *S. mutans* [3], and polymerization shrinkage, which creates marginal microgaps that facilitate bacterial invasion, acid penetration, and microleakage [4]. Consequently, passive restorations cannot effectively prevent further destruction of adjacent dental hard tissues.

To address these biological limitations, research on dental restorative materials has increasingly focused on antibacterial DCRMs designed to reduce bacterial adhesion and biofilm formation at the tooth-restoration interface [5]. These materials are intended to complement established preventive measures, providing an additional local defense against bacterial colonization in patients at increased caries risk [6]. Current strategies include release-based systems, which incorporate antimicrobial agents such as silver nanoparticles, zinc oxide or copper nanoparticles, chlorhexidine, and antibiotics, as well as contact-active systems based on immobilized antibacterial compounds [5].

Among contact-active strategies, quaternary ammonium (QA) monomers have attracted considerable attention. The most notable example is 12-methacryloyloxydodecylpyridinium bromide (MDPB) [7,8], the only QA monomer

commercially used in dentistry [9]. However, as a monomethacrylate, MDPB reduces crosslink density and compromises the mechanical and physicochemical properties of the resin matrix [10]. Therefore, MDPB is used only as a functional additive at low concentrations in adhesive systems [9] and is not suitable as the primary resin matrix component.

To overcome the limitations of antibacterial monomethacrylates, current research has focused on dimethacrylates with quaternary ammonium (QA) groups, which may enable the formation of highly crosslinked polymer networks while providing antibacterial activity without compromising the physicochemical and mechanical properties required for dental applications [11,12]. Several monomers of this type have been developed, including derivatives of N-methyldiethanolamine (MDEA) [13,14], N,N-dimethylaminoethyl methacrylate (DMAEMA) [15,16], bisphenol A diglycidyl ether derivatives [17], aliphatic and cycloaliphatic urethane-dimethacrylates [18,19], and betulin-based dimethacrylates [20]. Studies have demonstrated that their copolymerization with conventional dental dimethacrylate resins effectively inhibits bacterial growth. However, their incorporation is frequently associated with increased cytotoxicity and deterioration of the physico-mechanical properties of the resulting materials [11-20]. Therefore, simultaneous optimization of monomer chemical structure and resin matrix composition remains essential for developing DCRMs with balanced biological and functional performance.

To address these challenges, our group developed a series of quaternary ammonium urethane-dimethacrylates (QAUDMAs) differing in both the diisocyanate (DI) core and the length of the N-alkyl substituent (QAn) (Figure 1).

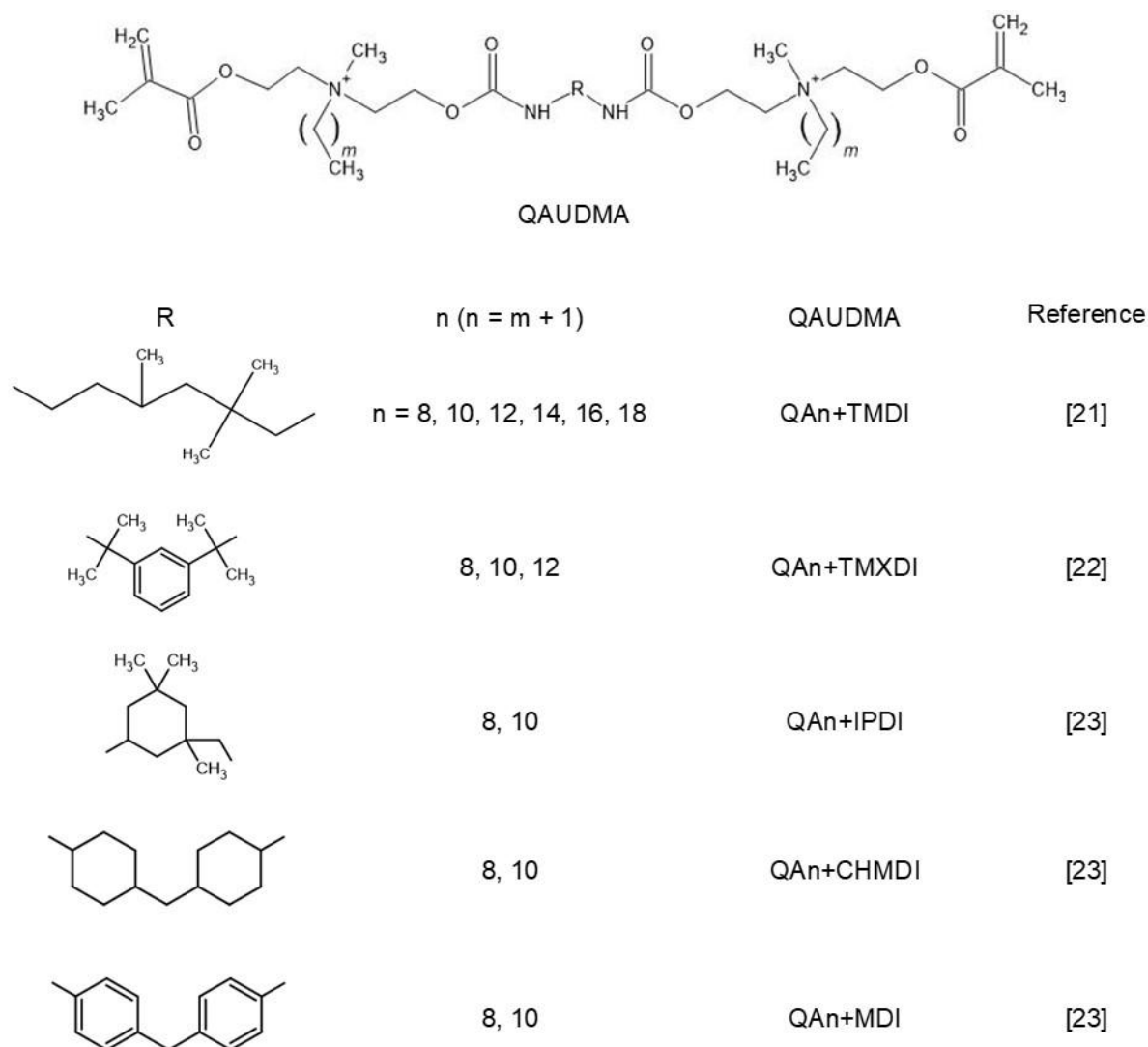


Fig 1 Chemical structures of the QAUDMA monomer series

Initially, QAUDMAs were synthesized using 2,2,4-(2,4,4-)trimethylhexamethylene diisocyanate (TMDI) and various 2-(methacryloyloxy)ethyl-2-hydroxyethylmethylalkylammonium bromides (QAHAMA-n) (QAn+TMDI; QA8-QA18) [21]. The obtained QAn+TMDIs were subsequently used to modify a conventional dental resin matrix composed of Bis-GMA 40 wt.%, UDMA 40 wt.%, and TEGDMA 20 wt.% (Figure 2) by complete replacement of the UDMA component. The resulting copolymers (40(QAn+TMDI)_{ps}) exhibited promising mechanical properties and antibacterial activity,

particularly in systems containing shorter alkyl substituents (QA8–QA12) [24]. Nevertheless, 40(QA8+TMDI)_p and 40(QA10+TMDI)_p demonstrated excessive *WS* (68.27 and 48.42 $\mu\text{g}/\text{mm}^3$, respectively [25], Figure 3a), exceeding the ISO 4049:2019 limit of 40 $\mu\text{g}/\text{mm}^3$ [26]. In contrast, 40(QA12+TMDI)_p combined acceptable water sorption (35.54 $\mu\text{g}/\text{mm}^3$ [25]) with favorable mechanical properties and antibacterial activity [24]. These findings indicated that modifying only the alkyl chain length was insufficient to optimize both antibacterial performance and stability in an aqueous environment.

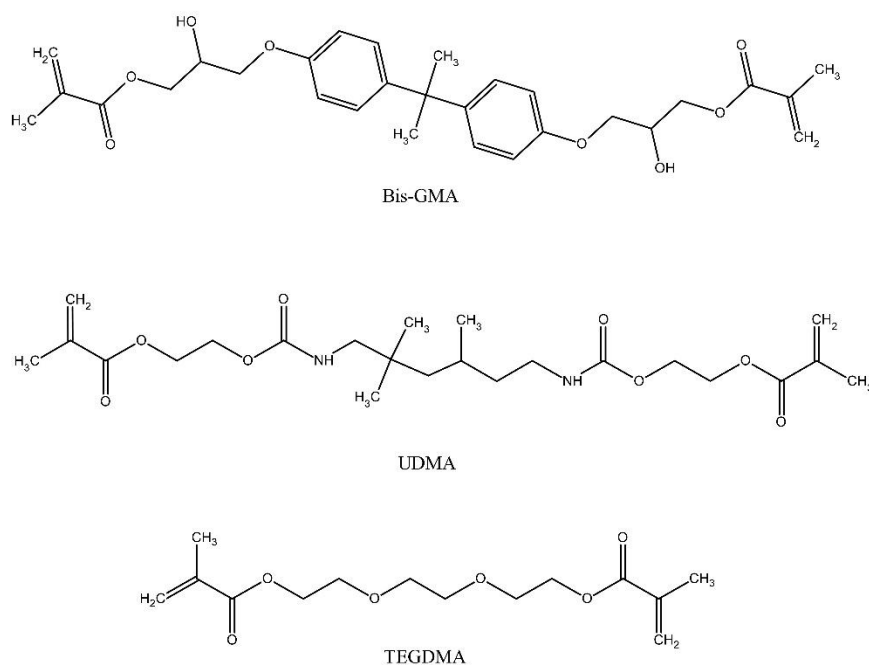


Fig 2 Chemical structures of common dental dimethacrylates: Bis-GMA, UDMA, and TEGDMA [27]

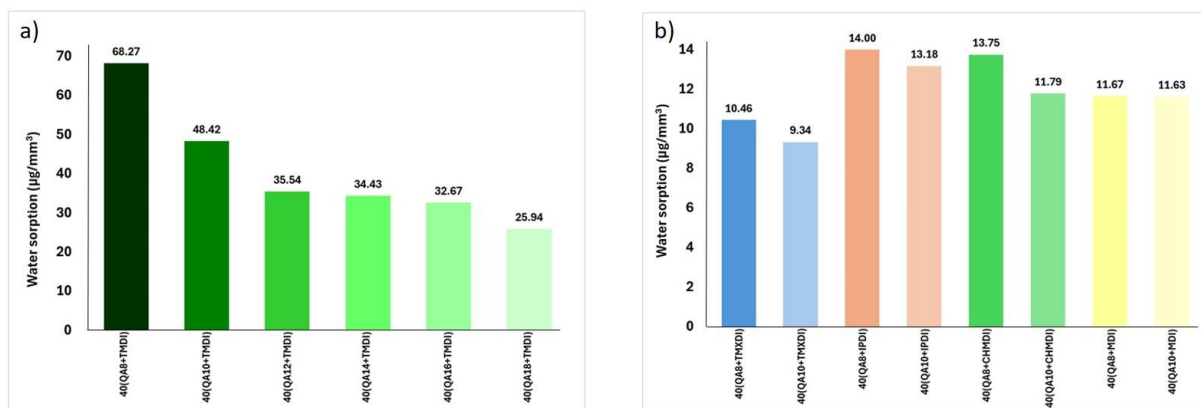


Fig 3 Water sorption (WS) of 40(QAUDMA)_pS: a) based on QAn+TMDI, with QA8-QA18 (data taken from [25]), b) based on QAn+DI, with QA8 or QA10 and TMXDI, IPDI, CHMDI, or MDI (data taken from [23] and [28])

Subsequent studies focused on reducing WS , which was considered the main limitation of 40(QAn+TMDI)_pS. QAUDMAs containing QA8 or QA10 and different DI-derived cores (TMXDI, IPDI, CHMDI, or MDI) were synthesized. Incorporation of cycloaliphatic or aromatic rings reduced WS of the resulting 40(QAUDMA)_pS to 9.34-14.0 $\mu\text{g}/\text{mm}^3$ [23,28] (Figure 3b), well below the ISO 4049:2019 limit [26].

However, despite extensive research on antibacterial dental resin matrices containing QA-based dimethacrylates, the influence of their molecular structure on the overall polymer performance has not been systematically investigated. Therefore, this study systematically compares TMXDI-, IPDI-, CHMDI-, and MDI-based 40(QAUDMA)_pS to determine how DI chemical structure affects their physicochemical, mechanical, antibacterial, and preliminary cytocompatibility properties, to establish a structure-property relationships that can guide the rational design of antibacterial resin matrices for dental composite applications.

To achieve this objective, comprehensive characterization was performed for both the monomer formulations and the corresponding copolymers. Monomer formulations were evaluated in terms of viscosity (η), density (d_m), and refractive index (RI). In contrast, the

copolymers were characterized with respect to density (d_p), degree of conversion (DC), polymerization shrinkage (S), glass transition temperature (T_g), flexural strength (FS), modulus (E), hardness (HB), *in vitro* antibacterial activity against *S. mutans*, and *in vitro* biological response of L-929 fibroblasts. The results were compared with a conventional 40(UDMA)_p dental resin matrix.

2. Methods

2.1. Chemicals and reagents

Methyl methacrylate (MMA), MDEA, decyl bromide (DB), and octyl bromide (OB) were purchased from Acros Organics (Geel, Belgium). Bis-GMA, camphorquinone (CQ), CHMDI, DMAEMA, IPDI, MDI, phenothiazine (PTZ), TEGDMA, TMXDI, and UDMA were obtained from Sigma-Aldrich (St. Louis, MO, USA). Dibutyltin dilaurate (DBTDL) was purchased from Fluka (Charlotte, NC, USA). Magnesium sulfate and potassium carbonate were obtained from Chempur (Piekary Śląskie, Poland). Dichloromethane, trichloromethane, and toluene were purchased from Stan-lab (Lublin, Poland). *S. mutans* (ATCC 33535), mouse fibroblasts (L-929 cell line, NCTC clone 929; ATCC CCL-1), MTT reagent, and dimethyl sulfoxide (DMSO) were obtained from ATCC (Manassas, VA, USA). Tryptic soy broth (TSB) was purchased from Biomaxima (Poland), and Columbia agar from bioMérieux (Marcy l'Étoile, France).

2.2. QAUDMA synthesis

QAUDMAs were synthesized according to a previously reported procedure [21-23] (Figure 4).

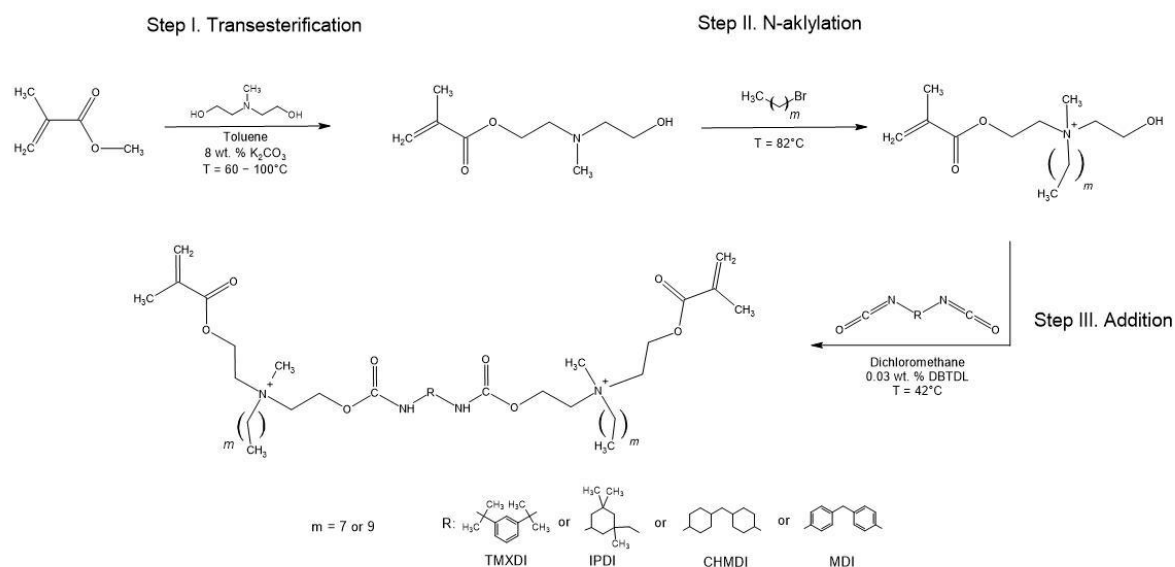


Fig 4 Synthesis route of experimental QAUDMAs

First, N,N-(2-hydroxyethyl)methylaminoethyl methacrylate (HAMA) was obtained by transesterification of MMA with MDEA using potassium carbonate 8 wt.% (catalyst) and PTZ 500 ppm (inhibitor). The reaction was carried out in toluene (solvent) at 60-100 °C for 2.5 h. It was followed by successive extraction with water and chloroform, and purification by vacuum distillation (3 mbar). HAMA was then subjected to N-alkylation with OB and DB to yield 2-(methacryloyloxy)ethyl-2-hydroxyethylmethyloctylammonium bromide (QAHAMA-8) and 2-(methacryloyloxy)ethyl-2-decylhydroxyethylmethylammonium bromide (QAHAMA-10), respectively. The reaction was carried out at 82 °C for 90 h. Subsequently, QAHAMA-8 or QAHAMA-10 was reacted with TMXDI, IPDI, CHMDI, or MDI using DBTDL 0.03 wt.% (catalyst) and PTZ 500 ppm (inhibitor) in a 50% methylene chloride solution at 42 °C for 5 h. Eight QAUDMAs were obtained: QA8+TMXDI, QA10+TMXDI, QA8+IPDI, QA10+IPDI, QA8+CHMDI, QA10+CHMDI, QA8+MDI, and QA10+MDI (Figure 1). After solvent removal (30 mbar), the monomers were post-cured overnight to complete the addition reaction. Structures were confirmed by ^1H and ^{13}C NMR, and peak assignments were reported previously [21-23].

2.3. Curing

Experimental monomer formulations consisted of QAUDMA 40 wt.%, Bis-GMA 40 wt.%, and TEGDMA 20 wt.% (40(QAUDMA)_{ms}). A reference formulation, 40(UDMA)_m, containing UDMA 40 wt.% instead of QAUDMA, was also prepared. All formulations were enriched with CQ 0.4 wt.% (initiator) and DMAEMA 1 wt.% (co-initiator), poured into molds, covered with a poly(ethylene terephthalate) film, and irradiated in a 4 mm-thick layer under a UV–Vis lamp (Ultra Vitalux 300, Osram, Germany; 280–780 nm, 2400 mW/cm²) for 1 h, as described in our previous studies [22–25]. After curing, the specimens were ground to obtain the final dimensions required for individual tests. Bar-shaped specimens measuring 64 × 10 × 3 mm (length × width × thickness) and disc-shaped specimens measuring 40 × 4 mm (diameter × thickness) and 10 × 3 mm (diameter × thickness) were prepared.

2.4. Properties of monomer formulations

The d_m was measured at 23 °C using a pycnometer, according to the ISO 1675:2022 standard [29], η was determined at 40 °C using a B-One Plus viscometer with a small-volume adapter (Lamy Rheology, Champagne-au-Mont-d’Or, France), according to the ISO 2555:2018 standard [30], and RI was measured at 23 °C using a DR 6100T refractometer (Krüss Optronic, Hamburg, Germany), according to the ISO 489:2022 standard [31].

2.5. Physicochemical properties of copolymers

The d_p was measured using an AS 60/220.X2 Plus analytical balance (Radwag, Poland) with a density measurement kit and, together with d_m , used to calculate S according to the following equation:

$$S (\%) = \left(1 - \frac{d_m}{d_p}\right) \times 100 \quad (1)$$

The DC in copolymers was determined using a Spectrum Two Fourier transform infrared spectrometer (FTIR, Perkin Elmer, USA). Monomers were analyzed as thin films between KBr pellets, while copolymers were analyzed as powders (<100 μ m) dispersed in

KBr. Spectra were recorded at 1 cm⁻¹ resolution (128 scans). The *DC* was calculated from the following equation:

$$DC = 1 - \frac{\left(\frac{A_{C=C}}{A_{Ar}}\right)_{40(QAUDMA)_p}}{\left(\frac{A_{C=C}}{A_{Ar}}\right)_{40(QAUDMA)_m}} \quad (2)$$

where, $A_{C=C}$ – absorption of aliphatic C=C at 1637 cm⁻¹, A_{Ar} – absorption of aromatic skeletal vibrations at 1607 cm⁻¹.

The T_g of copolymers was determined using a DSC 3 differential scanning calorimeter (Mettler Toledo, Switzerland) at 10 K/min over the temperature range of 0-200°C in an air atmosphere. T_g value was taken as the midpoint of the transition, according to the ISO 11357-2:2020 standard [32].

2.6. Mechanical properties of copolymers

The *FS* and *E* of copolymers were measured using a Zwick Z020 universal testing machine (Germany) on bar-shaped specimens (64 × 10 × 3 mm; length × width × thickness), according to the ISO 178:2019 standard [33], and calculated according to the following equations:

$$E \text{ (MPa)} = \frac{P_1 l^3}{4bd^3\delta}, \quad (3)$$

$$FS \text{ (MPa)} = \frac{3Pl}{2bd^2}, \quad (4)$$

Where, P – the maximum load, P_l – the load at the selected point of the elastic region of the stress-strain plot, l – the distance between supports ($l = 48$ mm), b – the sample width, d – the sample thickness, δ – the deflection of the sample at P_l .

The *HB* was determined according to ISO 2039-1:2001 [34] using the ball indentation method with a VEB Werkstoffprüfmaschinen tester (Germany) on disc-shaped specimens (40 mm × 4 mm; diameter × thickness) and calculated according to the following equation:

$$HB \text{ (MPa)} = \frac{F_m \frac{0.21}{(h - h_r) + 0.21}}{\pi d h_r}, \quad (5)$$

Where, F_m – the test load, d – the diameter of the ball indenter ($d = 5 \text{ mm}$), h – the immersion depth, h_r – the reduced depth of immersion ($h_r = 0.25 \text{ mm}$).

2.7. *In vitro* antibacterial activity of copolymers

In vitro antibacterial activity was evaluated against *S. mutans* (ATCC 33535, USA) by measuring bacterial adhesion to disc-shaped copolymer specimens (10 mm × 3 mm; diameter × thickness). Samples were incubated with a bacterial suspension ($\sim 5 \times 10^6 \text{ CFU/mL}$) at 37 °C for 18 h. After incubation, the specimens were rinsed with sterile water and transferred into 1 mL of sterile water, then vortexed at 3000 rpm for 1 min to detach adhered bacteria. Serial dilutions were prepared using 0.9% NaCl solution, and 100 μL aliquots were plated on blood agar plates. The plates were incubated at 37 °C for 18 h, and colonies were counted to determine the number of adherent bacteria.

2.8. *In vitro* cytocompatibility of copolymer extracts

In vitro biological response was assessed using the MTT assay with L-929 mouse fibroblasts (ATCC CCL-1, USA). Extracts were prepared according to ISO 10993-12 [35] and cell viability was evaluated according to ISO 10993-5:2009 [36] using the MTT assay. Sterilized disc-shaped copolymer specimens (10 mm × 3 mm; diameter × thickness) were incubated in culture medium (EMEM supplemented with 10% horse serum, penicillin 100 IU/mL, and streptomycin 100 $\mu\text{g/mL}$) for 2 and 10 days to obtain extracts. L-929 cells were seeded into 96-well plates at a density of $1 \times 10^4 \text{ cells/well}$ and exposed for 24 h to extracts diluted 1:1 with culture medium, followed by MTT staining and absorbance measurement at 550 nm using an Eon spectrophotometer (BioTek, USA). Cell viability was calculated according to the following equation:

$$Cell\ viability\ (\%) = \frac{A}{A_c} \times 100\% \quad (6)$$

where A – the absorbance of tested extracts, A_c – the absorbance of a control

Copolymers with viability $\geq 70\%$ were considered non-cytotoxic.

2.9. Statistical Analysis

Statistical analysis was performed using the Wilcoxon test in Statistica 13.3 (TIBCO Software, USA) for five samples, with significance set at $p = 0.05$. Results are presented as the mean with corresponding standard deviation (SD).

3. Results

3.1. Properties of monomer formulations

Eight experimental 40(QAUDMA)_ms and one reference 40(UDMA)_m monomer formulations were prepared: 40(QA8+TMXDI)_m, 40(QA10+TMXDI)_m, 40(QA8+IPDI)_m, 40(QA10+IPDI)_m, 40(QA8+CHMDI)_m, 40(QA10+CHMDI)_m, 40(QA8+MDI)_m, 40(QA10+MDI)_m, and 40(UDMA)_m, and tested for physicochemical properties (Table 1).

The η ranged from 4.04 to 18.19 Pa·s and increased in the order IPDI < CHMDI < TMXDI < MDI. Within each DI series, QA8 formulations were more viscous than their QA10 counterparts (5.61–18.19 vs. 4.04–12.11 Pa·s). Compared with 40(UDMA)_m (1.11 Pa·s), the viscosities of 40(QAUDMA)_ms were approximately 3-16 times higher, depending on the DI structure. Most differences were statistically significant ($p \leq 0.05$), except between 40(QA10+TMXDI)_m and 40(QA8+CHMDI)_m.

The d_m ranged from 1.12 to 1.19 g/cm³, with the lowest values found for 40(QA10+TMXDI)_m and 40(QA10+CHMDI)_m, and the highest for 40(QA8+MDI)_m and 40(QA10+MDI)_m. These values differed significantly from most other systems ($p \leq 0.05$). QA8 formulations generally exhibited higher d_m than QA10, although these differences were not statistically significant ($p > 0.05$). The d_m of 40(UDMA)_m (1.11 g/cm³) was comparable to

most QAUDMA formulations but remained approximately 4-7% lower than that of the MDI-based systems ($p \leq 0.05$).

The RI ranged from 1.508 to 1.531, increasing in the order $TMXDI < IPDI < CHMDI < MDI$, with all $40(QAUDMA)_m$ s showing higher values than $40(UDMA)_m$ (1.505). No consistent trend was observed between the QA8 and QA10 series. All RI results were statistically significant ($p \leq 0.05$).

Table 1 Properties of $40(QAUDMA)_m$ s: viscosity (η), density (d_m), and refractive index (RI)

	$40(QA8+TMXDI)_m$	$40(QA10+TMXDI)_m$	$40(QA8+IPDI)_m$	$40(QA10+IPDI)_m$	$40(QA8+CHMDI)_m$	$40(QA10+CHMDI)_m$	$40(QA8+MDI)_m$	$40(QA10+MDI)_m$	$40(UDMA)_m$
η (Pa·s)	9.37	7.79	5.61	4.04	7.66	4.83	18.19	12.11	1.11
	(0.12)	(0.14)	(0.06)	(0.11)	(0.09)	(0.08)	(0.05)	(0.22)	(0.06)
	a,i,j,k,l,m	b,i,p,q,r,s	c,j,p,u,v,	d,k,q,u,z,	e,l,v,z, δ , ϵ	f,m,r,w, α ,	g,n,s,x, β , ϵ ,	h,o,t,y, γ , ζ ,	a,b,c,d,e,f,
	,n,o	,t	w,x,y	α , β , γ	, ζ	δ , η , θ	η , λ	θ , λ	g,h
d_m	1.15	1.12	1.15	1.14	1.14	1.12	1.19	1.16	1.11
(g/cm ³)	(0.01)	(0.01)	(0.01)	(0.01)	(0.01)	(0.01)	(0.02)	(0.02)	(0.01)
	a,g,h,i	g,j,k,l,m	b,j,n,o	c,k,p,q	d,r	h,n,p,s,t	e,i,l,o,q,r,s	f,m,t	a,b,c,d,e,f
RI	1.508	1.514	1.519	1.517	1.520	1.519	1.531	1.528	1.505

Values are presented as mean and SD . Different letters indicate statistically significant differences among formulations ($p \leq 0.05$). No superscript letters were assigned for RI values because all comparisons were statistically significant ($p \leq 0.05$).

3.2. Physicochemical properties of copolymers

The monomer formulations were photocured to obtain 40(QAUDMA)_ps:
 40(QA8+TMXDI)_p, 40(QA10+TMXDI)_p, 40(QA8+IPDI)_p, 40(QA10+IPDI)_p,
 40(QA8+CHMDI)_p, 40(QA10+CHMDI)_p, 40(QA8+MDI)_p, 40(QA10+MDI)_p, and
 40(UDMA)_p. Copolymers were tested for physicochemical properties (Table 2).

Table 2 Physicochemical properties of 40(QAUDMA)_ps: density (d_p), polymerization shrinkage (S), degree of conversion (DC), and glass transition temperature (T_g)

	40(QA8+TMXDI) _p	40(QA10+TMXDI) _p	40(QA8+IPDI) _p	40(QA10+IPDI) _p	40(QA8+CHMDI) _p	40(QA10+CHMDI) _p	40(QA8+MDI) _p	40(QA10+MDI) _p	40(UDMA) _p
d_p	1.22	1.20	1.20	1.20	1.20	1.19	1.22	1.19	1.20
(g/cm ³)	(0.02)	(0.01)	(0.01)	(0.01)	(0.01)	(0.01)	(0.01)	(0.01)	(0.01)
	a,e,f,g	h	i	j	e	b,f,k	c,h,i,j,k,l	d,g,l	a,b,c,d
S (%)	6.27	6.68	4.68	4.53	4.84	5.71	2.45	3.45	7.42
	(0.95)	(1.01)	(0.78)	(1.03)	(0.85)	(0.66)	(0.81)	(0.88)	(1.08)
	g,h,i,j,k	l,m,n,o,p	a,g,l,q	b,h,m,r,s	c,i,n,t,u	d,r,t,v,w	e,j,o,q,s,u,v	f,k,p,w	a,b,c,d,e,f
DC	0.74	0.71	0.63	0.65	0.59	0.59	0.59	0.62	0.59
	(0.09)	(0.09)	(0.06)	(0.04)	(0.04)	(0.03)	(0.03)	(0.02)	(0.06)
	a,b,c,d,e,f,g	h,i,j,k,l,m	b,h,n	c,i,o,p,q	d,j,n,o	e,k,p	f,l,q,r	g,m,r	a
T_g (°C)	64.0	65.0	59.3	60.6	59.9	60.0	61.6	61.5	62.8
	(1.3)	(1.3)	(0.7)	(0.9)	(1.3)	(0.7)	(0.6)	(0.9)	(1.8)
	c,d,e,f,g,h	i,j,k,l,m,n	a,c,i,o,p	d,j,q	b,e,k	f,l,r,s	g,m,o,q,r	h,n,p,s	a,b

Values are presented as mean (SD). Different letters indicate statistically significant differences among copolymers ($p \leq 0.05$).

The d_p ranged from 1.19 to 1.22 g/cm³. 40(QA10+CHMDI)_p and 40(QA10+MDI)_p showed the lowest d_p values, while 40(QA8+TMXDI)_p and 40(QA8+MDI)_p showed the highest, with both extremes differing significantly from each other and from the intermediate d_p of 40(UDMA)_p (1.20 g/cm³) ($p \leq 0.05$). QA8 copolymers usually showed higher d_p values than the corresponding QA10 systems, except for the IPDI pair. In most cases, the differences were not significant ($p > 0.05$), except for the MDI pair, where a significant difference was observed.

The S of 40(QAUDMA)_ps ranged from 2.45 to 6.68%, increasing in the order MDI < IPDI < CHMDI < TMXDI, with significant differences between the MDI and TMXDI copolymers ($p \leq 0.05$), while 40(UDMA)_p showed the highest S (7.42%), significantly exceeding MDI systems ($p \leq 0.05$) but not differing from TMXDI copolymers ($p > 0.05$). Although QA8 copolymers typically exhibited lower S than QA10, most differences were not statistically significant ($p > 0.05$), except for CHMDI.

The DC ranged from 0.59 to 0.74, with the highest values for TMXDI copolymers. The lowest were for both CHMDI copolymers and 40(QA8+MDI)_p, significantly lower than others ($p \leq 0.05$). Most QA8 and QA10 differences were not significant ($p > 0.05$), except for MDI ($p \leq 0.05$). The DC of 40(UDMA)_p (0.59) was similar to most 40(QAUDMA)_ps, except for 40(QA8+TMXDI)_p, which had a DC ~25% higher ($p \leq 0.05$).

The T_g values ranged from 59.3 to 65.0 °C, with TMXDI copolymers showing significantly higher values, compared to other 40(QAUDMA)_ps ($p \leq 0.05$). The lowest T_g was for IPDI and CHMDI copolymers, which were significantly lower than those of TMXDI and MDI copolymers. No significant effect of N-alkyl chain length was observed ($p > 0.05$). The T_g of 40(UDMA)_p (62.8 °C) was comparable to most 40(QAUDMA)_ps ($p > 0.05$) but significantly higher than 40(QA8+IPDI)_p and 40(QA8+CHMDI)_p ($p \leq 0.05$).

3.3. Mechanical properties of copolymers

40(QAUDMA)_ps were also tested for mechanical properties (Table 3).

Table 3 Mechanical properties of 40(QAUDMA)_ps: modulus (*E*), flexural strength (*FS*), hardness (*HB*)

	40(QA8+TMXDI) _p	40(QA10+TMXDI) _p	40(QA8+IPDI) _p	40(QA10+IPDI) _p	40(QA8+CHMDI) _p	40(QA10+CHMDI) _p	40(QA8+MDI) _p	40(QA10+MDI) _p	40(UDMA) _p
<i>E</i>	3.4	3.1	3.5	3.2	3.0	2.6	3.1	3.0	3.6
(GPa)	(0.3)	(0.2)	(0.2)	(0.2)	(0.2)	(0.1)	(0.2)	(0.3)	(0.2)
	f,g	a,h,i	h,j,k,l,m,n	j,o,p,q	b,f,k,o,r	c,g,i,l,p,r,s,t	d,m,s,	e,n,q,t	a,b,c,d,e
<i>FS</i>	73.6	73.6	69.8	67.0	71.0	68.1	68.9	70.07	95.6
(MPa)	(5.6)	(6.6)	(7.2)	(3.7)	(4.9)	(7.3)	(5.1)	(7.1)	(5.2)
	a,i	b	c	d,i	e	f	g	h	a,b,c,d,e,f,g,h
<i>HB</i>	99.4	98.8	92.5	95.5	91.3	98.3	83.3	86.6	109.4
(MPa)	(2.5)	(3.5)	(3.9)	(1.2)	(1.0)	(1.3)	(7.0)	(4.8)	(4.6)
	a,i,j,k,l,m	b,n,o,p	c,i,q	d,j,r,s,t,u	e,k,n,r,v,w	f,q,s,v,x,y	g,l,o,t,w,x	h,m,p,u,y	a,b,c,d,e,f,g,h

Values are presented as mean and (*SD*). Different letters indicate statistically significant differences among copolymers ($p \leq 0.05$).

The *E* ranged from 2.6 to 3.5 GPa. The highest values were observed for IPDI copolymers and 40(QA8+TMXDI)_p ($p > 0.05$), while the lowest was found for 40(QA10+CHMDI)_p, differing significantly from the remaining 40(QAUDMA)_ps ($p \leq 0.05$). QA8 copolymers generally exhibited slightly higher *E* values than their QA10 counterparts,

although most differences were not significant except for CHMDI ($p \leq 0.05$). 40(UDMA)_p (3.6 GPa) showed an E value comparable to the IPDI copolymers and 40(QA8+TMXDI)_p ($p > 0.05$), but significantly higher than the remaining 40(QAUDMA)_{ps} ($p \leq 0.05$).

The FS ranged from 67.0 to 73.6 MPa, with TMXDI copolymers showing the highest values. Significant differences were observed only between 40(QA8+TMXDI)_p and 40(QA10+IPDI)_p ($p \leq 0.05$). N-alkyl chain length had little effect on FS ($p > 0.05$). All 40(QAUDMA)_{ps} showed significantly lower FS than the reference 40(UDMA)_p, with the strongest copolymers exhibiting an approximate 22% reduction ($p \leq 0.05$).

The HB ranged from 83.3 to 99.4 MPa, with TMXDI copolymers having the highest values and MDI copolymers showing the lowest ($p \leq 0.05$). Differences between QA8 and QA10 were minor ($p > 0.05$), except for CHMDI ($p \leq 0.05$). The reference 40(UDMA)_p (109.4 MPa) had significantly higher HB than all 40(QAUDMA)_{ps} ($p \leq 0.05$), with a maximum HB reduction of approximately 10% for the hardest systems.

3.4. *In vitro* antibacterial activity of copolymers

The antibacterial activity of the copolymers was evaluated by assessing *S. mutans* adhesion. No bacterial colonies were observed on any of the 40(QAUDMA)_{ps}, indicating complete inhibition of bacterial adhesion. In contrast, 40(UDMA)_p exhibited high bacterial counts in the undiluted suspension (3562 ± 338 CFU/mL), which decreased progressively with dilution, reaching zero at a 1:100 dilution.

3.5. *In vitro* cytocompatibility of copolymer extracts

Biocompatibility was evaluated through L-929 fibroblast viability (Table 4).

After 2 days, viability for the 40(QAUDMA)_{ps} ranged from 47% to 116%. Most copolymers had viability above 70%, except 40(QA8+CHMDI)_p (47%). 40(QA8+TMXDI)_p and 40(QA10+TMXDI)_p showed the highest viability (112 and 116%, respectively) both significantly higher than other 40(QAUDMA)_{ps} ($p \leq 0.05$) and comparable to 40(UDMA)_p

(114%, $p > 0.05$). The effect of the N-alkyl substituent was less pronounced after 2 days, noted only for CHMDI (97 and 47% for 40(QA10+CHMDI)_p and 40(QA8+CHMDI)_p, respectively, $p \leq 0.05$). After 10 days, cell viability decreased for most 40(QAUDMA)_ps, ranging from 36% to 84%, while 40(UDMA)_p reached 108%. Significant changes were observed for TMXDI copolymers, 40(QA8+IPDI)_p, and 40(QA8+CHMDI)_p ($p \leq 0.05$). Only 40(QA8+CHMDI)_p (36%) and 40(QA8+IPDI)_p (37%) fell below the 70% viability threshold and showed the lowest values. QA8 copolymers usually exhibited lower viability than their QA10 counterparts ($p \leq 0.05$), except for MDI, where no significant difference was observed ($p > 0.05$).

Table 4 Cell viability of 40(QAUDMA)_ps after 2 and 10 days

Incubation time (days)	Cell viability (%)								
	40(QA8+TMXDI) _p	40(QA10+TMXDI) _p	40(QA8+IPDI) _p	40(QA10+IPDI) _p	40(QA8+CHMDI) _p	40(QA10+CHMDI) _p	40(QA8+MDI) _p	40(QA10+MDI) _p	40(UDMA) _p
2	112 (7) f,g,h,i A	116 (5) j,k,l,m,n,o B	85 (11) a,f,j,p C	75 (15) b,g,k,q D	47 (6) c,h,l,p,q,r D	97 (14) d,m,r	91 (18) n,s	83 (18) e,i,o,t	114 (12) a,b,c,d,e
10	70 (5) a,i,j,k,l A	84 (3) b,i,m,n,o B	37 (3) c,j,m,p,q,r,s C	77 (5) d,p,t,u,v D	36 (2) e,k,n,t,w, x,y D	86 (4) f,l,o,q,u,w,z ,α	76 (6) g,r,v,x,z	79 (8) h,s,y,α	108 (4) a,b,c,d,e,f,g,h

Values are presented as mean (*SD*). Different lowercase letters indicate statistically significant differences among copolymers within rows, whereas different uppercase letters indicate significant differences within columns ($p \leq 0.05$).

4. Discussion

This study explored the influence of DI structure (specifically TMXDI, IPDI, CHMDI, and MDI) and N-alkyl substituent length (QA8 and QA10) on the properties of monomer compositions and their copolymers formulated with Bis-GMA 40 wt.%, QAUDMA (Figure 1) 40 wt.%, and TEGDMA 20 wt.%. This approach involved completely replacing UDMA 40 wt.% in a conventional DCRM matrix, allowing for direct comparison with a well-established dental reference system. This strategy identified 40(QAUDMA)_ps that match the 40(UDMA)_p reference in key physicochemical and mechanical properties, while also exhibiting high antibacterial activity with satisfactory cytocompatibility. Ultimately, the study demonstrated that DI structure is the primary factor governing 40(QAUDMA)_p behavior, with N-alkyl chain length playing a complementary role.

The influence of DI structure on the properties of 40(QAUDMA)_ms (Table 1) was most evident in η . The highest η was observed for aromatic MDI-based formulations, likely because the planar conformation of the benzene ring promotes efficient packing and stronger intermolecular interactions. In contrast, cycloaliphatic DIs (IPDI, CHMDI) resulted in lower η , attributed to steric hindrance and greater molecular flexibility. TMXDI caused intermediate behavior despite containing a benzene ring, consistent with an aliphatic character of this DI. In comparison, d_m and RI varied less significantly, although MDI-based formulations showed the highest values, suggesting greater molecular organization and higher polarizability associated with aromatic structures. The QA8/QA10 substitution exerted a secondary effect. QA8 systems generally showed slightly higher η and d_m , likely due to reduced intermolecular

spacing and more efficient packing. RI was minimally affected, indicating limited influence of alkyl chain length on optical properties. Compared with the 40(UDMA)_m reference, all 40(QAUDMA)_{ms} exhibited substantially higher η due to the more complex molecular structure. However, RI remained within the clinically acceptable range (~ 1.47 – 1.52 [37]), with only MDI-based systems slightly exceeding this range (~ 1.53), suggesting good potential for optical compatibility with fillers and favorable aesthetic performance.

DI-dependent effects were also evident in the physicochemical properties of 40(QAUDMA)_{ps} (Table 2). TMXDI-based copolymers exhibited the highest DC together with elevated T_g and controlled S , indicating efficient network formation resulting from a balance between rigidity and chain mobility. In contrast, MDI-based copolymers showed the lowest DC and S , suggesting that the high rigidity of aromatic structure may limit polymerization efficiency despite relatively high T_g values. IPDI- and CHMDI-based systems showed intermediate behavior consistent with their cycloaliphatic structures. The effect of QA chain length remained minor, indicating that QA8/QA10 substitution acts mainly as a local modifier rather than a determinant of global network structure. Compared with the 40(UDMA)_p reference, most 40(QAUDMA)_{ps} showed reduced S and comparable or higher DC , indicating improved volumetric stability without compromising polymerization efficiency. Their T_g values remained similar to the reference, suggesting preservation of thermal material stability.

Mechanical properties (Table 3) of 40(QAUDMA)_{ps} were primarily governed by DI structure. TMXDI- and IPDI-based copolymers exhibited the highest E . TMXDI systems also showed the highest FS and HB . In these systems, the presence of a benzene ring contributed to increased stiffness. At the same time, the aliphatic character maintained sufficient chain mobility for efficient crosslinking, resulting in well-developed networks and effective stress distribution. CHMDI-based copolymers demonstrated the weakest mechanical performance,

likely due to steric hindrance associated with two cyclohexane rings. MDI-based systems showed relatively high stiffness resulting from a rigid aromatic structure, although their lower *DC* limited full network development. The influence of QA chain length on mechanical performance was limited. QA10 systems tended to exhibit slightly lower *E*, suggesting increased flexibility due to longer alkyl chains acting as internal plasticizers. However, *FS* and *HB* were only minimally affected, indicating that local structural changes did not substantially alter global network behavior. Compared with the 40(UDMA)_p reference, the mechanical properties of 40(QAUDMA)_ps were moderately reduced, likely due to the lower crosslink density associated with the presence of two bulky QA groups and the increased spacing between the polymerizable double bonds in QAUDMA molecules. Nevertheless, most copolymers showed higher *E*, *FS*, and *HB* than another conventional dental copolymer consisting of Bis-GMA 60 wt.% and TEGDMA 40 wt.% (*E* ~ 2.8 GPa, *FS* ~ 55 MPa, *HB* ~ 60 MPa [24]), confirming that incorporation of QA groups and rigid DI structures did not compromise mechanical performance to a clinically unacceptable level. Overall, TMXDI-based copolymers exhibited the most favorable mechanical profile, combining high stiffness, hardness, and flexural strength. MDI-based systems also showed relatively high stiffness due to their aromatic structure, although lower *DC* reflected limited network formation. In contrast, CHMDI-based copolymers demonstrated the weakest mechanical properties, while IPDI-based systems showed intermediate behavior.

The antibacterial activity of QA-containing polymers is primarily attributed to contact-active interactions between permanently charged QA groups and negatively charged bacterial membranes. Because the QA moieties are covalently incorporated into the polymer network, antibacterial activity depends on surface-exposed cationic sites rather than the continuous release of antimicrobial agents [38]. Consistent with this mechanism, all 40(QAUDMA)_ps completely inhibited *S. mutans* adhesion, whereas the reference 40(UDMA)_p showed no

antibacterial activity, confirming the effectiveness of the incorporated QA functionality. Since bacterial adhesion was entirely suppressed in all experimental groups, no DI- or QA-dependent differences could be distinguished under the applied test conditions. These findings suggest that future optimization should focus on reducing the QAUDMA content while maintaining sufficient surface density of QA groups to preserve antibacterial efficacy.

While all 40(QAUDMA)_{ps} exhibited complete inhibition of *S. mutans* adhesion, the incorporation of antibacterial functionality should not compromise the biological response of host tissues. However, a major challenge in developing antibacterial resins is the trade-off between antimicrobial efficacy and biological safety, as higher biocide concentrations usually lead to impaired cytocompatibility [39]. Therefore, the cytocompatibility of the experimental copolymers was evaluated using L-929 fibroblasts. The results demonstrated a generally favorable biological response (Table 4), with most 40(QAUDMA)_{ps} exceeding the 70% viability threshold defined by ISO 10993-5:2009 [36] after both 2 and 10 days, suggesting an acceptable safety profile under physiological conditions. However, time-dependent effects revealed differences between systems. TMXDI-based copolymers exhibited the highest initial cell viability, comparable to the reference material, followed by a significant decrease over time. Importantly, their viability remained above the cytotoxicity threshold after 10 days, indicating preserved biocompatibility. Given their high *DC*, the observed cytotoxic response likely reflects a more realistic release profile of residual components rather than delayed or diffusion-limited effects. 40(QA8+IPDI)_p and 40(QA8+CHMDI)_p showed significant reductions in viability (36-37%) after prolonged incubation, suggesting increased release of cytotoxic species. In contrast, MDI-based systems showed relatively stable viability, although their lower *DC* may indicate restricted diffusion of residual monomers rather than genuinely improved biocompatibility. Consequently, variations in cell viability highlight an important difference between the two systems: TMXDI-based copolymers, due to their higher *DC*,

provide a more transparent and representative assessment of biological response, whereas MDI-based systems may exhibit partially “masked” cytotoxicity associated with restricted release of residual components and may lead to an underestimation of cytotoxic potential under the applied test conditions. Longer alkyl chains (QA10) generally improved viability, probably due to increased hydrophobicity limiting diffusion of toxic species.

Overall, TMXDI-based systems provided the best balance of antibacterial activity, physicochemical stability, mechanical performance, and cytocompatibility. MDI-based systems represented a secondary option, combining good stiffness with potentially diffusion-limited release of residual species. The results further suggest that reducing QAUDMA content in 40(QAUDMA)_ps may improve long-term biocompatibility while preserving antibacterial effectiveness, representing the next stage of formulation optimization.

5. Conclusions

DI structure strongly influenced the physicochemical, mechanical, and biological properties of 40(QAUDMA)_ps, while QA chain length had a secondary effect. TMXDI-based copolymers showed the best overall balance of polymerization efficiency, mechanical performance, shrinkage control, and cytocompatibility. MDI-based systems exhibited high stiffness but lower *DC*, indicating limiting network formation, whereas IPDI and CHMDI systems showed intermediate and the least favorable properties, respectively. All 40(QAUDMA)_ps completely inhibited *S. mutans* adhesion, confirming strong antibacterial activity. Cytocompatibility was generally acceptable, although time-dependent effects indicated that network formation and residual diffusion significantly affect biological response. Overall, DI selection enables effective tuning of QAUDMA-based copolymers, with TMXDI-based systems being the most promising for further development.

Abbreviations

40(QA10+CHMDI) _m	Monomer formulation containing 40 wt.% QA10+CHMDI
40(QA10+CHMDI) _p	Copolymer prepared from 40(QA10+CHMDI) _m
40(QA10+IPDI) _m	Monomer formulation containing 40 wt.% QA10+IPDI
40(QA10+IPDI) _p	Copolymer prepared from 40(QA10+IPDI) _m
40(QA10+MDI) _m	Monomer formulation containing 40 wt.% QA10+MDI
40(QA10+MDI) _p	Copolymer prepared from 40(QA10+MDI) _m
40(QA10+TMXDI) _m	Monomer formulation containing 40 wt.% QA10+TMXDI
40(QA10+TMXDI) _p	Copolymer prepared from 40(QA10+TMXDI) _m
40(QA8+CHMDI) _m	Monomer formulation containing 40 wt.% QA8+CHMDI
40(QA8+CHMDI) _p	Copolymer prepared from 40(QA8+CHMDI) _m
40(QA8+IPDI) _m	Monomer formulation containing 40 wt.% QA8+IPDI
40(QA8+IPDI) _p	Copolymer prepared from 40(QA8+IPDI) _m
40(QA8+MDI) _m	Monomer formulation containing 40 wt.% QA8+MDI
40(QA8+MDI) _p	Copolymer prepared from 40(QA8+MDI) _m
40(QA8+TMXDI) _m	Monomer formulation containing 40 wt.% QA8+TMXDI
40(QA8+TMXDI) _p	Copolymer prepared from 40(QA8+TMXDI) _m
40(UDMA) _m	Reference monomer formulation containing 40 wt.% UDMA
40(UDMA) _p	Reference copolymer prepared from 40(UDMA) _m
A_{Ar}	Absorbance of aromatic skeletal vibrations
$A_{C=C}$	Absorbance of aliphatic C=C stretching vibrations
ATCC	American Type Culture Collection
b	Sample width
Bis-GMA	Bisphenol A-glycidyl methacrylate
CHMDI	Dicyclohexylmethane-4,4'-diisocyanate

CQ	Camphorquinone
d	Sample thickness
d_m	Monomer density
d_p	Copolymer density
DB	Decyl bromide
DBTDL	Dibutyltin dilaurate
DC	Degree of conversion
DCRM	Dental composite restorative material
DI	Diisocyanate
DMAEMA	N,N-Dimethylaminoethyl methacrylate
DMSO	Dimethyl sulfoxide
E	Flexural modulus
FS	Flexural strength
HAMA	N,N-(2-Hydroxyethyl)methylaminoethyl methacrylate
HB	Ball indentation hardness
IPDI	Isophorone diisocyanate
ISO	International Organization for Standardization
l	Distance between supports ($l = 48$ mm)
L-929	Mouse fibroblast cell line (NCTC clone 929)
m	Monomer formulation
MDEA	N-Methyldiethanolamine
MDI	Diphenylmethane-4,4'-diisocyanate
MDPB	12-Methacryloyloxydodecylpyridinium bromide
MMA	Methyl methacrylate
MTT	3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide

NMR	Nuclear magnetic resonance
OB	Octyl bromide
p	Polymer/copolymer
<i>P</i>	Maximum load
<i>P_l</i>	Load at the selected point of the elastic region of the stress-strain plot
PTZ	Phenothiazine
QA	Quaternary ammonium
QA8	Octyl-substituted quaternary ammonium compound
QA10	Decyl-substituted quaternary ammonium compound
QA12	Dodecyl-substituted quaternary ammonium compound
QAn	Quaternary ammonium compound with an N-alkyl substituent
QAHAMA-n bromide	2-(Methacryloyloxy)ethyl-2-hydroxyethylmethyl-n-alkylammonium bromide
QAUDMA	Quaternary ammonium urethane-dimethacrylate
<i>RI</i>	Refractive index
<i>S</i>	Polymerization shrinkage
<i>S. mutans</i>	Streptococcus mutans
TEGDMA	Triethylene glycol dimethacrylate
<i>T_g</i>	Glass transition temperature
TMDI	2,2,4-(2,4,4-Trimethylhexamethylene) diisocyanate
TMXDI	Tetramethylxylene diisocyanate
TSB	Tryptic soy broth
UDMA	Urethane-dimethacrylate
<i>WS</i>	Water sorption
δ	Sample deflection at P1

Declarations**Ethics Approval**

Not applicable.

Consent for Participation and Publication

Not applicable.

Availability of Data and Materials

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing Interests

The authors declare that they have no competing interests.

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Authors' Contributions

IBR: Conceptualization; Project administration; Funding acquisition; Writing – review and editing. PD: Methodology; Investigation; Formal analysis; Data curation; Visualization; Writing – original draft. GC: Methodology; Investigation; Formal analysis; Data curation. AM: Methodology; Investigation; Formal analysis; Data curation. All authors read and approved the final manuscript.

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Clinical Trial Registration

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