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Title: Development of new diacrylate monomers as substitutes for Bis-GMA and UDMA
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Abstract:

Objective: Bis-GMA and UDMA that are widely used as main components of (meth) acrylic monomer compositions. However, the application of Bis-GMA which is a bisphenol A derivative was doubted in dentistry, after bisphenol A was revealed to have estrogenic activity. Although UDMA has considered as a substitute for Bis-GMA, the mechanical properties of cured resin composite containing UDMA are still insufficient. Therefore, in this study, I developed new alternative (meth) acrylic monomers to enhance the mechanical strength of cured products of composite resins.

Methods: As a (meth) acrylic monomer substituted for Bis-GMA and UDMA, five urethane acrylic monomers were synthesized in this study. Elastic modulus, strength and breaking energy were measured through three points flexural test of cured resin from (meth) acrylic monomer mixture of the urethane acrylates and TEGDMA.

Result: Three points flexural test of cured resin revealed that the newly synthesized urethane acrylates excels in a balance of mechanical properties, such as rigidity and toughness as compared with the cured UDMA -based resin.

Conclusion: The new urethane diacrylates, TMXDI-HEA, TMXDI-HPA, XDI-HPA and NBDI-HEA, can be useful for restorative resin composites to substitute Bis-GMA and UDMA.

Keywords: dental monomer, bending test, high strength dental materials, diacrylate monomer, urethane acrylates, composite resin, light curing resins

1. Introduction

Resin composites are widely used as tooth color restorative materials in dental restoration, and basically contain a (meth) acrylic monomer composition and additives such as a filler, a polymerization initiator, a polymerization inhibitor, and etc. [1]. In a composite resin including such components, a filler usually has the largest weight fraction, followed by a (meth) acrylic monomer composition and these two components represent a major proportion of the weight of the composite resin[2]. The (meth) acrylic monomer composition serves as a binder for the filler. The properties of monomers, and the properties of cured products of the compositions are significantly influential on the properties and performance of the resin composites containing the monomer composition, and cured products thereof [3].

From the points of view of aspects such as the biological safety of monomers and the mechanical strength and wear resistance of cured products, the (meth) acrylic monomer compositions frequently include radically polyfunctional methacrylates. Typically, the polyfunctional methacrylate compositions are based on Bisphenol A diglycidyl methacrylate (hereinafter, written as Bis-GMA) or dimethacryloxyethyl 2,2,4-trimethylhexamethylene diurethane (hereinafter, written as UDMA) [3]. Bis-GMA was incorporated into composite dental resins in 1962 by Rafael Bowen, and is still a resin most commonly used in dental composite, dental sealants and dental cement [4]. It is the diester derived from methacrylic acid and the bisphenol A diglycidyl ether [5]. Bearing two polymerizable groups, it is prone to form a crosslinked polymer that is used in dental restorations. However, Bis-GMA also has a potential problem resulted in one of its base material, bisphenol A which is an endocrine disruptor [6, 7]. In addition, due to considerably high viscosity of Bis-GMA, a low viscosity monomer, such as triethyleneglycol dimethacrylate (TEGDMA), is always incorporated in order for Bis-GMA to be practically useful as base resins for resin composites [8, 9]. However, high amount of TEGDMA incorporation leads to increased polymerization shrinkage, water sorption and reduced mechanical properties [10].

As an alternative dimethacrylate monomer for Bis-GMA, UDMA has been widely used to prepare Bis-GMA free dental resin composites [1, 11, 12]. However, the mechanical properties of cured resin composite containing UDMA are still insufficient [13]. In particular, the poor strength obstructs the application of the resins to sites subjected to a high stress, for example, the use as molar tooth crowning materials.

In view of the problems discussed above, the aim of this study was to provide dental (meth) acrylic monomer compositions that can give cured products having high mechanical properties

2. Materials and Methods

2.1. Synthesis monomers

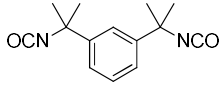
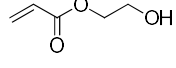
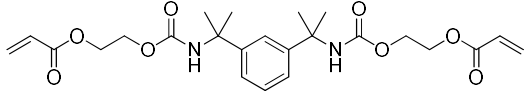
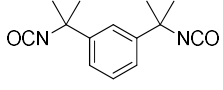
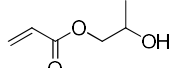
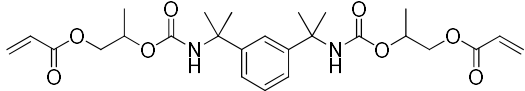
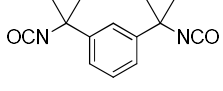
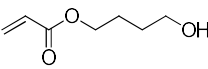
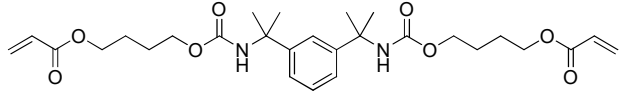
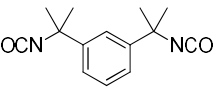
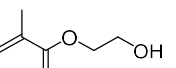
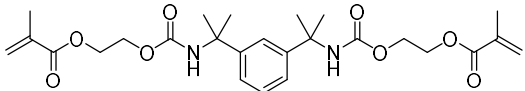
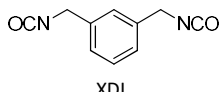
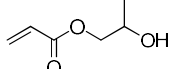
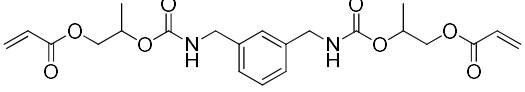
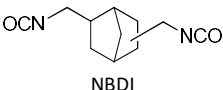
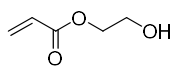
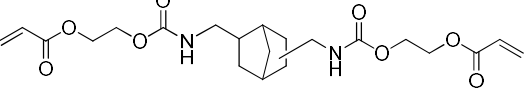
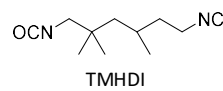
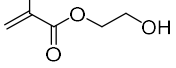
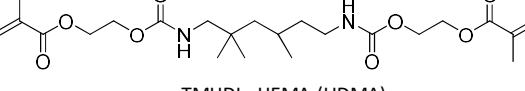
A thoroughly dried 1-liter four-necked flask equipped with a stirring blade and a thermometer was loaded with 270.0 g (2.325 mol) of 2-hydroxyethyl acrylate (HEA), 0.55 g of dibutyltin dilaurate (DBTDL) (0.1 wt% relative to the total weight of HEA and 1,3-Bis(1-isocyanato-1-methylethyl)benzene (TMXDI)) and 0.28 g of BHT (0.05 wt% relative to the total weight of HEA and TMXDI). The mixture was stirred to uniformity and was thereafter heated to 60°C. Subsequently, 284.0 g (1.163 mol) of TMXDI was added dropwise over a period of 1 hour. The dropwise addition was accompanied by an increase in inside temperature due to the reaction heat, and thus the rate of the dropwise addition was controlled so that the temperature did not exceed 80°C. After the whole amount had been added dropwise, the reaction was performed for 10 hours while keeping the reaction temperature at 80°C. During this process, the progress of the reaction was tracked by HPLC analysis to determine the end point of the reaction. The product was discharged from the reactor. In this manner, 530 g of a urethane acrylate TMXDI – HEA was obtained.



Scheme 1 Synthesis of TMXDI – HEA

Urethane (meth)acrylates were synthesized from hydroxyalkyl (meth)acrylates and diisocyanates illustrated in Table 1 under similar conditions with that of TMXDI – HEA as shown above. Bis-GMA was purchased from Shin-Nakamura Chemical Co., Ltd.

Table 1 Urethane (meth)acrylates synthesized in this study

Diisocyanates	Hydroxyallyl (meth)acrylates	Urethane (meth)acrylates
 TMXDI	 HEA	 TMXDI - HEA
 TMXDI	 HPA	 TMXDI - HPA
 TMXDI	 HBA	 TMXDI - HBA
 TMXDI	 HEMA	 TMXDI - HEMA
 XDI	 HPA	 XDI - HPA
 NBDI	 HEA	 NBDI - HEA
 TMHDI	 HEMA	 TMHDI - HEMA (UDMA)

2.2. Bending test

10.0 g (21.3 mmol) of the urethane acrylate TMXDI-HEA obtained in Production Example 1 and 4.53 g (15.8 mmol) of triethylene glycol dimethacrylate (TEGDMA) were added into a container. The mixture was stirred to uniformity at 50°C to give a (meth) acrylic monomer solution.

TMXDI - HEA have two acryloyl groups and TEGDMA have two methacryloyl groups. Thus, the proportion of the number of the acryloyl groups from TMXDI - HEA was 57% relative to the total number of the (meth)acryloyl groups in the (meth) acrylic monomer solution.

0.5 w% camphorquinone (CQ) and 0.5 w% 2-butoxyethyl 4-(dimethylamino)benzoate (DMAB2-BE) were added to the (meth) acrylic monomer solution. The mixture was stirred to uniformity at room temperature to give a dental polymerizable monomer composition. The dental polymerizable monomer composition was filled in a 2 x 2 x 25 mm stainless steel mold and was irradiated with light from a visible light irradiator (Solidilite V, SHOFU, Kyoto, Japan) for 3 minutes on each side, namely, for a total of 6 minutes on both sides. The specimens were removed from the mold and were heat treated in an oven at 110°C for 15 minutes. After that the specimens was cooled to room temperature. Thereafter, the specimen was soaked in distilled water in a closable sample bottle and was stored at 37°C for 24 hours. The specimen thus obtained was subjected to testing.

The specimens fabricated in the above manners were subjected to a three-point bending test using universal testing machine (AUTOGRAPH EZ-S, Shimadzu Corporation, Kyoto, Japan) under conditions in which the distance between the supports was 20 mm and the cross head speed was 1 mm/min.

Evaluation of the urethane (meth)acrylates synthesized in this study has been performed under the same conditions described above.

Data were analyzed with one-way ANOVA and post hoc Tukey HSD tests ($p < 0.05$).

2.3. Measurement of viscosity

The viscosity of the urethane (meth)acrylates was measured with a cone-plate viscometer (TVE-22H manufactured by TOKI SANGYO CO., LTD.). The temperature was controlled at 65°C with use of a circulation thermostatic tank.

2.4. Measurement of refractive index

The refractive index of the urethane (meth)acryl monomers were measured at 589nm and 23 °C using an Abbe's refractometer (DR-M2 manufactured by ATAGO CO., LTD.).

3. Results

TMXDI and 1, 3-bis(isocyanatomethyl)benzene (XDI), which have an aromatic ring and norbornane diisocyanate (NBDI), which has an aliphatic ring were selected as a suitably rigid diisocyanate for the study. The diisocyanates were reacted with hydroxyalkyl acrylates, for example, HEA, 2-hydroxy propyl acrylate (HPA) and 4-hydroxybutyl acrylate (HBA) to give urethane acrylates in table 1. The urethane acrylates contains rigid structure, an aromatic ring or aliphatic ring from the

diisocyanates.

A similar structure urethane methacrylate, TMXDI - HEMA was also synthesized from reaction of TMXDI and HEMA in a similar manner. UDMA was obtained from reaction of trimethylhexamethylene diisocyanate (TMHDI) and 2-hydroxyethyl methacrylate (HEMA) under similar conditions. TMHDI does not contain any aromatic or aliphatic ring in the molecular structure.

Elastic modulus, strength and breaking energy measured through three points flexural test of cured resins from (meth) acrylic monomer mixture of the urethane acrylates and TEGDMA were respectively shown in Figure 1-3. As controls, UDMA and TMXDI – HEMA was tested under the same conditions. Elastic modulus of the cured resin compositions containing TMXDI – HEA, TMXDI – HPA, XDI - HPA and NBDI – HEA were significantly higher than that of the cured resin composition containing UDMA. Regarding strength, the TMXDI – HEA –based resin was significantly superior and to that the UDMA –based resin. The cured resin compositions containing TMXDI – HPA, XDI - HPA and NBDI had better strength than the cured resin compositions containing UDMA. Standard deviation of breaking energy from the experiments was large, therefore statistical difference between breaking energy of these all samples was not observed. These results indicate that the cured resins from the new urethane acrylates excels in a balance of mechanical properties as compered with the cured resin from UDMA.

TMXDI – HEMA is a methacrylate monomer which has very similar structure to TMXDI – HEA. Difference between TMXDI – HEMA and TMXDI – HEA is only polymerizable functional groups. Regarding elastic modulus, strength of the cured resins, properties of TMXDI – HEMA and TMXDI – HEA were similar. Although statistically speaking, braking energy of each of the cured resin compositions containing TMXDI – HEA or TMXDI – HPA did not show significant difference, average breaking energy of TMXDI – HEA –based resin seems higher than that of TMXDI – HEMA –based.

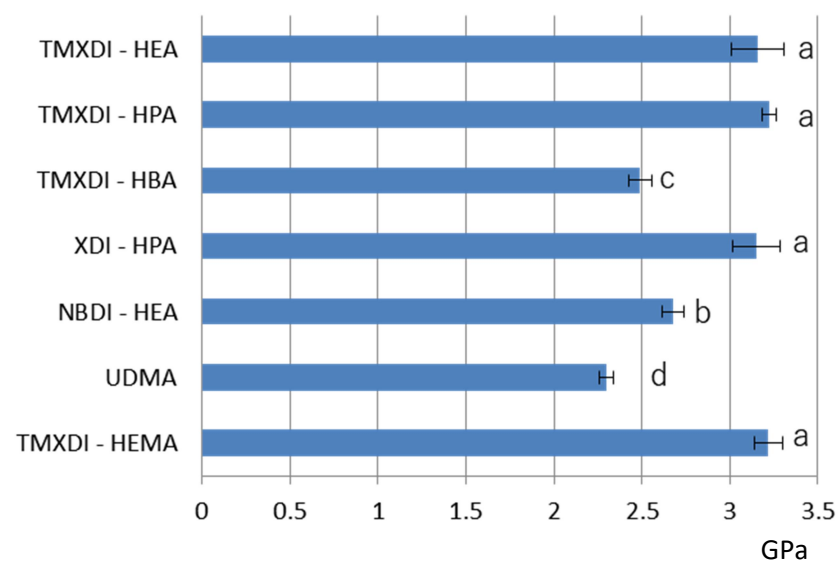


Figure 1 Elastic modulus of the cured resin compositions from the urethane (meth)acrylates and TEGDMA.

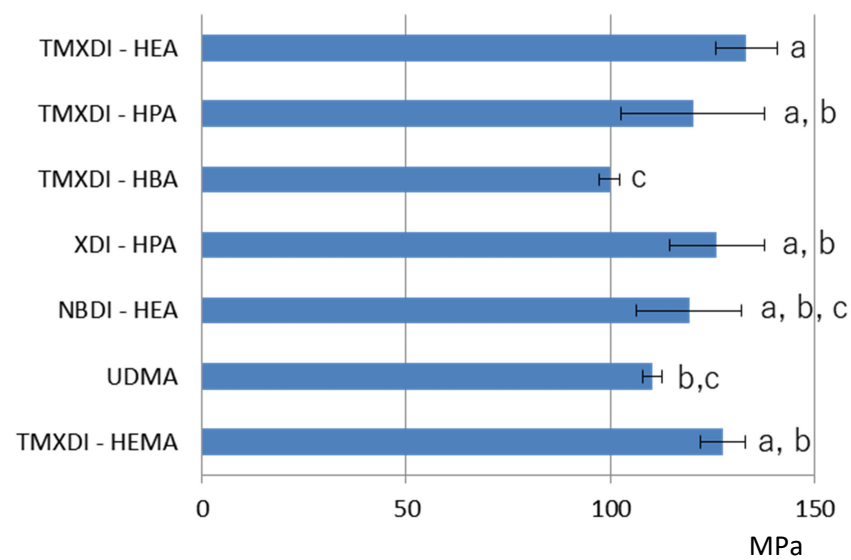


Figure 2 Strength of the cured resin compositions from the urethane (meth)acrylates and TEGDMA.

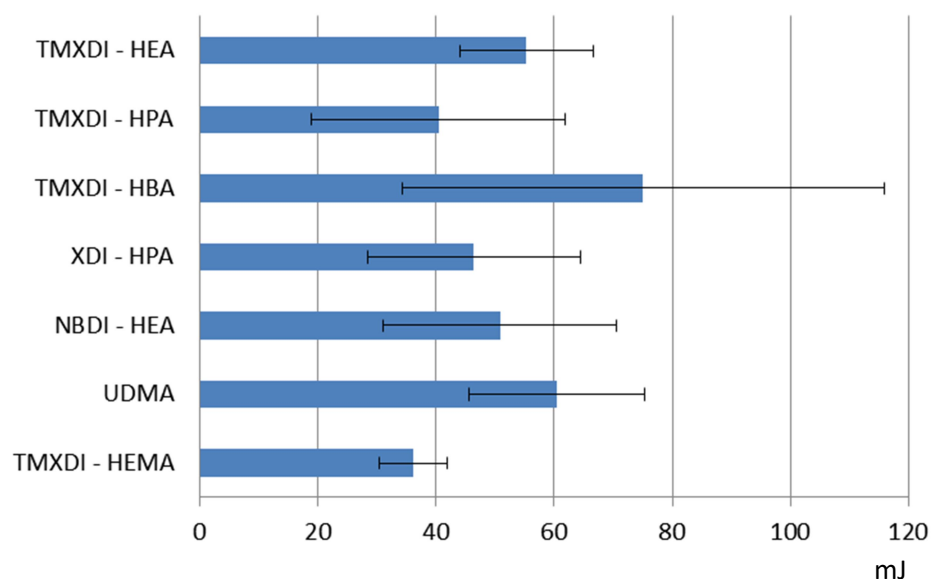


Figure 3 Breaking energy of the cured resin compositions from the urethane (meth)acrylates and TEGDMA.

Test results of viscosity of the urethane (meth)acrylates and Bis-GMA were displayed in Table 2. Viscosity of the new urethane acrylates was higher than that of UDMA, but was lower than that of Bis-GMA.

Table 2 Viscosity of the urethane (meth)acrylates and Bis-GMA

Monomers	Viscosity
	(mPa·s at 65 °C)
TMXDI – HEA	1670
TMXDI – HPA	1800
TMXDI – HBA	410
XDI – HPA	570
NBDI – HEA	930
UDMA	320
TMXDI – HEMA	1900
Bis-GMA	3660

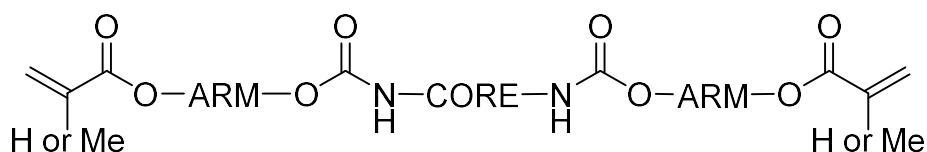
Refractive index of three urethane (meth)acrylates, UDMA and Bis-GMA were shown in Table 3. Urethane acrylate including an aromatic and aliphatic ring had higher much refractive index compared with UDMA.

Table 3 Refractive index of urethane (meth)acrylates and Bis-GMA

Urethane (meth)acrylates	Refractive index of monomer
TMXDI – HEA	1.517
XDI – HPA	1.515
NBDI – HEA	1.506
UDMA	1.484
Bis-GMA	1.551

4. Discussion

To develop new (meth)acrylates monomers as substitutes for Bis-GMA and UDMA, I synthesized urethane (meth)acrylates from hydroxyalkyl (meth)acrylates and diisocyanates. General structure of the monomers synthesized in this study is shown in Figure 4.

**Figure 4** General structure of urethane (meth)acrylate monomers

Central moiety between two carbamate groups of the molecule was derived from isocyanates (hereinafter, written as CORE). Outside from carbamate groups were derived from hydroxyalkyl (meth)acrylates and hereinafter, alkyl chains between a carbamate group and an ester group is called as ARM in the study.

UDMA does not have rigid structure, for examples, aromatic and aliphatic rings in the molecule structure [12]. Especially C6 aliphatic chain is considered as soft structure compared with an aromatic or aliphatic ring therefore the cured resin composition containing UDMA is lack in elastic modulus and do not has so high strength [13].

On the other hand, urethane acrylates in the study contain rigid structure, which is an aromatic or aliphatic ring, in the molecules. As a concrete example, TMXDI – HEA has a phenyl ring in CORE moiety and ARM moieties are C2 aliphatic chain, which is moderate soft structure. To ensure that cured resin exhibit both rigidity and toughness, it would be necessary that the good balance between a rigid segment and a soft segment in the molecular. It seems that the balance is very severe because elastic

modulus and strength of the cured TMXDI – HBA –based resin dramatically dropped compared with those of the cured TMXDI – HEA –based resin and became similar level to UDMA despite molecular structure of TMXDI – HBA is similar with TMXDI – HEA except of ARM length, just C2 aliphatic chain extension.

Several attempts to apply urethane methacrylate monomers containing rigid structure, for example TMXDI – HEMA to dental materials have been reported. [14, 15, 16] However such monomers have not been widely used in the area at least. As shown above, cured TMXDI – HEMA –based resin was brittle compared with cured TMXDI – HEA –bases resin. From the viewpoint of balance between a rigid segment and a soft segment, combination of a phenyl ring in CORE and methacrylate groups would not be the best because methacrylate resin is harder than acrylate resin. Conventionally, acrylate monomers have not been common for dental materials compared with methacrylate monomers so far. However this study indicates that acrylate groups would be more suitable for molecules containing rigid structure in CORE.

Refractive index of the urethane acrylates in the study was much higher than that of UDMA because of an aromatic ring and an aliphatic ring in the molecule [17, 18]. Higher refractive index monomers would be widely usable materials for radiopaque dental composites [19]. Low viscosity of the urethane acrylates compared with that of Bis-GMA could avoid limitations of composition of dental materials [19,20].

It is concluded that the newly synthesized urethane diacrylates, TMXDI-HEA, TMXDI-HPA, XDI-HPA and NBDI-HEA, can be useful for restorative resin composites to substitute Bis-GMA and UDMA.

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