IADR GENERAL SESSION
CAPE TOWN, SOUTH AFRICA • JUNE 25-28, 2014

המחלקה להנדסת פלסטיקה
Plastics Engineering Dept.

SHENKAR — שנקר
ENGINEERING. DESIGN. ART. הנדסה. עיצוב. אמנות
The Pernick Faculty of Engineering הפקולטה להנדסה ע"ש פרניק

BJM LAB
B.J.M. Laboratories Ltd.

Final Presentation / Poster Number # 930

Bisphenol-A Free Alternatives For Dental Polymer-Based Materials

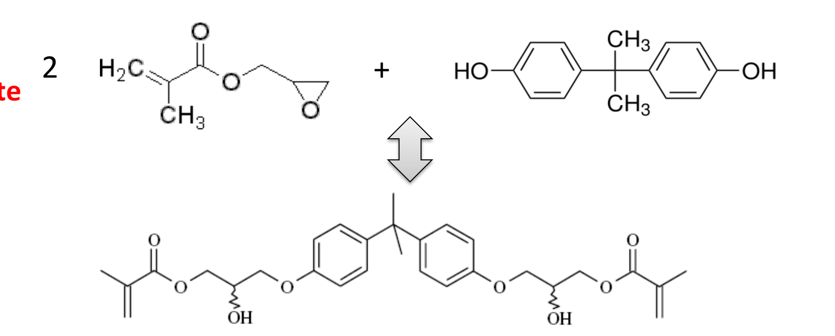
Kira Lizenboim [1], Hanna Dodiuk [2], Ira Suvorov [1], Barry Zalsman [1]

[1]B.J.M. Laboratories Ltd., Or Yehuda, ISRAEL
[2]Shenkar College, The Pernick Faculty of Engineering, Ramat Gan, ISRAEL

Rationale:

- Bisphenol-A (BPA) is suspected to be an endocrine disrupter (resembling Estrogen hormone)
- Current polymeric dental materials are based on BPA derivatives, e.g. Bisphenol-A Diglycidylether Methacrylate (Bis-GMA) which may leach out unreacted monomers and its degradation products
- The growing international concern regarding the presence of BPA in commercial products has led to many studies of its effect on human health
- However, this topic is still controversial because regulators think that the methods used in many of those studies haven't been fully validated

Glycidyl Methacrylate



BPA

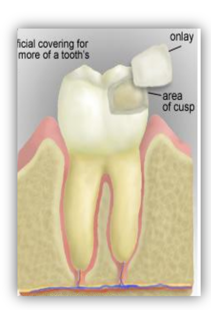
Bis-GMA

Objectives:

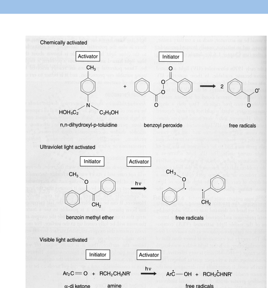
- To evaluate Bisphenol-A free alternatives for potential use in dental polymer-based materials:
  - Use of synthetic commercial oligomers
  - Newly synthesized monomers from renewable resources

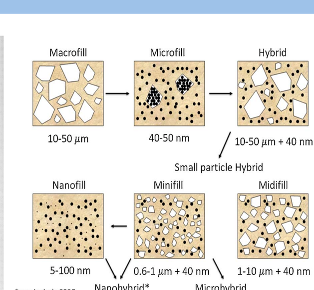
Introduction:

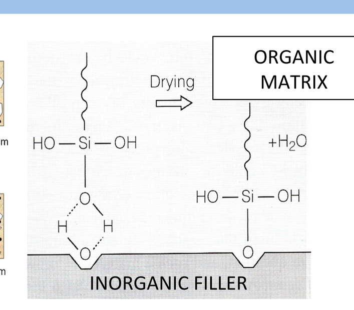
- Dental restorations
  - Repair a damaged tooth

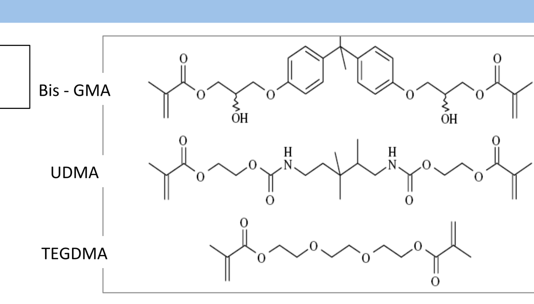


- Key properties:
  - Biocompatibility
  - Excellent bonding to tooth structure
  - Endurance within the aggressive oral environment
  - Dimensional stability
  - Easy handling and Dentist friendly
  - Matching natural tooth color







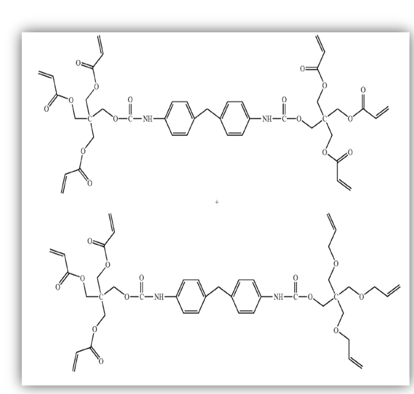


- The dental restorative system
  - Resin (BPA free)
  - Initiators
  - Fillers
  - Coupling agents (Resin - Filler)

Methods:

Synthetic Alternatives:

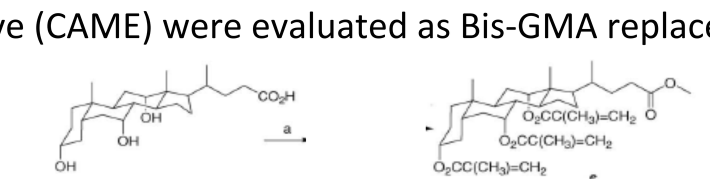
- 13 commercial oligomers produced by different manufacturers were studied as resins for dental composites:
  - Ethoxylated (4) Bisphenol A Dimethacrylate
  - Difunctional Polyester Acrylate
  - Difunctional Aliphatic Urethane Acrylates (DAUA)
  - Difunctional Aliphatic Urethane Methacrylate
  - Difunctional Aliphatic Polyester Tri-Urethane Acrylate
  - Urethane Di-Methacrylate
  - Trifunctional Aliphatic Polyester Urethane Acrylate
  - Isocyanurate
  - Glycerol Dimethacrlylate / Maleate
  - Urethane Dimethacrylate Elastomer
  - Hexafunctional Aliphatic Urethane Acrylate (HAlUA)
  - Hexafunctional Aromatic Urethane Acrylate (HArUA)



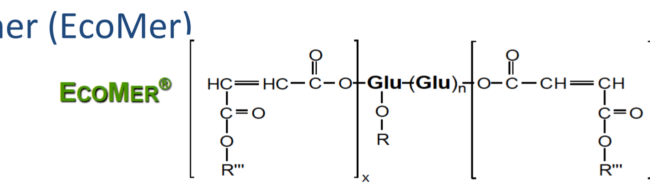
HArUA

Renewable Resource Monomers:

- Bile Acid (Cholic Acid)
  - Synthesis of a tri-methacrylate- monomer of cholic acid was carried out and verified by different methods as methacrylated derivative of cholic acid methyl ester (CAME)
  - The cholic acid derivative (CAME) were evaluated as Bis-GMA replacement



- Commercially available vinyl macromer (EcoMer)



Physical, mechanical and adhesive properties of HArUA , HAlUA and one of the two tested DAUA excelled in all formulations.

Testing Methods:

Nuclear Magnetic Resonance (NMR), FTIR, DSC - verification of the syntesized cholic acid derivative;

Compressive, Flexural, Shear Bond Strength; Water Sorption, Light Curing Time - Degree of Conversion, Shrinkage, Flow Properties – verification of composites and sealants.

All data was statistically analyzed by the analysis of variance (ANOVA) method, at a significance level set at $p<0.005$.

Preparation of Light Cure Composite and Sealant:

- 25 different composite formulations based on the five different oligomers:
  - Different ratios of Resin /Bis-GMA / TEGDMA (11-21)
  - Photoinitiator camphoroquinone (CQ) and accelerator ethyl-4-dimethylaminobenzoate (EDB) were added to the composite mixtures
  - Addition of the photoinitiators TPO and Irgacure 819 to the composite mixtures was evaluated
  - The Filler comprised fumed silica (Cab-O-Sil) and barium-aluminum-borosilicate glass powder (Dental Glass) of 4 different grinding sizes (0.4, 1.5, 6 μm and 180 nm) (F1-F5)
  - Hydroxyapatite (HAp) addition (nanostructured microparticles having specific surface area > 100 m^2/g) to the Filler mixture was evaluated (F6)
- The Filler content of the composites comprised of 3% untreated fumed silica (single particle size – 17nm, aggregate size 200-300nm) (Cab-O-Sil) and of 97% Dental Glass having a refractive index similar to the composite resin matrix (1.53) and treated with γ-Methacryloxypropyl-tri-methoxy-Silane. In some formulations 5% Dental Glass were replaced by 5% hydroxyapatite (HAp) (fine powder). Each formulation contained 75wt% of filler.
- Light cure dental composite restorative material ProFil, (made by Silmet Ltd.) was used as reference. ProFil contains Bis-GMA and TEGDMA resins and 75wt% glass filler.

- 3 different light cure pit & fissure sealant formulations based on three different oligomers containing photoinitiator camphoroquinone (CQ) and accelerator ethyl-4-dimethylaminobenzoate (EDB).
- Each sealant formulation contained 3wt% of untreated fumed silica (single particle size – 17nm, aggregate size 200-300nm) (Cab-O-Sil) **or** 5% hydroxyapatite (HAp) (fine powder) (nanostructured microparticles having specific surface area > 100 m2/g) as a filler.
- Light cure pit & fissure sealant Q-Seal, (made by B.J.M. Laboratories Ltd.) was used as reference. Q-Seal contains Bis-GMA and TEGDMA resins and 3wt% filler.

Results:

Fillers Compositions

Filler Mixture Number	Micron Particle Sizes (wt%)			Nano Particle Sizes (wt%)		HAp (wt%)	Total	μm/nm ratio
	Dental Glass (6μm)	Dental Glass (1.5μm)	Dental Glass (0.4μm)	Dental Glass (180nm)	Cab-O-Sil (17 nm)	HA (1μm)		
F1	97	0	0	0	3	0	100	32
F2	55	28	0	14 (0% Silane)	3	0	100	5
F3	55	28	0	14 (6% Silane)	3	0	100	5
F4	55	28	0	14 (13% Silane)	3	0	100	5
F5	43.4	32.6	21.6	0	2.4	0	100	41
F6	41.0	30.0	21.6	0	2.4	5.0	100	41

Adhesive and Mechanical Properties of Selected Oligomers / Filler Light Cure Pit & Fissure Sealant Formulations

Oligomer /Filler mixture description	Compressive Strength, MPa	Flexural Strength, MPa	Shear Bond Strength *to Etched Bovine Enamel*, Mpa / Failure Mode
HArUA:TEGDMA=80:20 / Cab-O-Sil	190 ± 36^{c}	200 ± 26^{b}	50 ± 6^{b} / Cohesive
HArUA:TEGDMA=80:20 / HAp	228 ± 19^{a}	185 ± 14^{a}	54 ± 9^{c} / Cohesive
DAUA:TEGDMA=80:20 / Cab-O-Sil	154 ± 27^{c}	191 ± 37^{c}	42 ± 5^{b} / Mixed
DAUA:TEGDMA=80:20 / HAp	330 ± 65^{c}	204 ± 42^{c}	49 ± 6^{a} / Cohesive
HAlUA:TEGDMA=80:20 / Cab-O-Sil	201 ± 28^{b}	228 ± 11^{a}	48 ± 6^{b} / Cohesive
HAlUA:TEGDMA=80:20 / HAp	244 ± 36^{b}	247 ± 20^{a}	49 ± 6^{b} / Cohesive
Q-Seal (Ref.)	191 ± 54^{c}	205 ± 33^{a}	45 ± 5^{a} / Cohesive

Standard deviations are ± (a) 10%, (b) 15% and (c) 20%. Values with the different superscript letters (a, b, c) in the same column are statistically different (p<0.005).

Mechanical Properties of Selected Oligomers / Fillers Light Cure Composite Formulations

containing photoinitiator CQ and accelerator EDB

Mixture number	Oligomer mixture number	Oligomer mixture description	Filler mixture number	Compressive Strength, MPa	Flexural Strength, MPa
11-F1	11	HArUA:TEGDMA:Bis-GMA	F1	202 ± 18^{a}	189 ± 33^{b}
11-F2	11	HArUA:TEGDMA:Bis-GMA	F2	257 ± 22^{a}	162 ± 23^{b}
11-F3	11	HArUA:TEGDMA:Bis-GMA	F3	236 ± 10^{a}	220 ± 21^{a}
11-F4	11	HArUA:TEGDMA:Bis-GMA	F4	135 ± 40^{a}	212 ± 35^{a}
11-F5	11	HArUA:TEGDMA:Bis-GMA	F5	260 ± 21^{a}	239 ± 31^{a}
12-F1	12	EBAD:TEGDMA:Bis-GMA	F1	180 ± 38^{b}	182 ± 8^{a}
13-F1	13	HArUA:TEGDMA=70:30	F1	149 ± 29^{b}	177 ± 20^{a}
13-F5	13	HArUA:TEGDMA=70:30	F5	272 ± 28^{a}	239 ± 31^{a}
14-F1	14	HArUA:TEGDMA=80:20	F1	167 ± 40^{c}	221 ± 14^{a}
14-F4	14	HArUA:TEGDMA=80:20	F4	181 ± 19^{a}	161 ± 28^{b}
14-F5	14	HArUA:TEGDMA=80:20	F5	294 ± 21^{a}	227 ± 13^{a}
14-F6	14	HArUA:TEGDMA=80:20	F6	245 ± 13^{a}	213 ± 30^{b}
15-F1	15	CAME:TEGDMA=60:40	F1	70 ± 8^{a}	110 ± 11^{a}
15-F5	15	CAME:TEGDMA=60:40	F5	130 ± 9^{a}	64 ± 12^{b}
16-F5	16	DAUA:TEGDMA=80:20	F5	246 ± 18^{b}	178 ± 15^{b}
16-F6	16	DAUA:TEGDMA=80:20	F6	229 ± 19^{c}	194 ± 18^{a}
17-F5	17	HAlUA:TEGDMA=80:20	F5	220 ± 18^{a}	217 ± 22^{a}
17-F6	17	HAlUA:TEGDMA=80:20	F6	223 ± 11^{a}	243 ± 26^{a}
ProFil (Ref.)				223 ± 33^{a}	274 ± 52^{b}

containing photoinitiator TPO in addition to CQ and EDB

14-F5	14	HArUA:TEGDMA=80:20	F5	238 ± 23^{a}	201 ± 35^{b}
16-F5	16	DAUA:TEGDMA=80:20	F5	238 ± 32^{b}	191 ± 14^{a}
17-F5	17	HAlUA:TEGDMA=80:20	F5	210 ± 22^{a}	210 ± 22^{a}

containing photoinitiator Irgacure 819 in addition to CQ and EDB

14-F5	14	HArUA:TEGDMA=80:20	F5	227 ± 38^{b}	199 ± 13^{a}
16-F5	16	DAUA:TEGDMA=80:20	F5	192 ± 21^{a}	171 ± 18^{a}
17-F5	17	HAlUA:TEGDMA=80:20	F5	250 ± 21^{a}	230 ± 14^{a}

Physical Properties of Investigated Bisphenol-A Free Dental Composites

Property	Standard Requirements	CAME based	HArUA based	HAlUA based	DAUA based
Biocompatibility	Material should show no cytotoxicity	N/E	N/E	N/E	N/E
Light curing time @ 23°C	Not more than 30 sec	20 sec	20 sec	20 sec	20 sec
Degree of Conversion, %	Degree of conversion should reach at least 50% 5 min after the start of irradiation by a visible light-curing lamp	44	45	76	40
Water sorption, $\mu g/mm^3$	Maximum 40 $\mu g/mm^3$	40	23	15	15
Solubility, $\mu g/mm^3$	Maximum 7.5 $\mu g/mm^3$	14	2	3	4
Flexural strength, MPa	Minimum 50 MPa	64	227	217	178
Compressive strength, MPa	Minimum 50 MPa	130	294	220	246
Radiopacity, % Al	Minimum 100 % Al	√	√	√	√
Adhesion (SBS to etched bovine enamel, MPa)	Minimum 15 MPa to etched enamel using a bonding agent	33	38	36	35
Volumetric shrinkage, %	Maximum 7 %	<3	<3	<3	<3
Wear resistance	Maximum volume loss of 10 μm per 39,000 3-body wear cycles	N/E	N/E	N/E	N/E
Handling propery: viscosity vs. shear rate	While the viscosity decreases under an increasing shear rate, once the force is removed, the viscosity should returns to nearly the higher viscosity	√	√	√	√
Shade (color) stability	Material should be visually homogeneous and match the defined color	√	√	√	√

Standard deviations are ± (a) 10%, (b) 15% and (c) 20%. Values with the different superscript letters (a, b, c) in the same column are statistically different (p<0.005).

N/E – Not Established in our laboratory.

Conclusions:

- The objective was to replace the Bis-GMA resin
- Maintain its key properties
- Changing as little as possible the composition (Resin/TEGDMA ratios, initiators and filler)
- The experimental results showed that Bis-GMA can be substituted by
  - Tri-methacrylated derivative of cholic acid methyl ester (referred to as CAME)
  - Aromatic-urethane hexafunctional oligomer (HArUA)
  - Hexafunctional Aliphatic Urethane Acrylate (HAlUA)
  - Difunctional Aliphatic Urethane Acrylates (DAUA)