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CROSS-LINKED ACRYLIC BONE CEMENT WITH BIODEGRADABLE ADDITIVES

ŠĶĒRSSAIŠU SATUROŠS AKRILA KAULU CEMENTS AR BIODEGRADĒJOŠĀM PIEDEVĀM

Visvaldis Vitins, *leading researcher, Dr.sc.ing.,*
Riga Technical University, Institute of Biomaterials and Biomechanics.
Address: Azenes str. 14/24, Riga, LV-1048, Latvia.
E-mail: vvitins@inbox.lv

Ivars Knets, *professor, Dr.hab.sc.ing.,*
Riga Technical University, Institute of Biomaterials and Biomechanics.
Address: Azenes str. 14/24, Riga, LV-1048, Latvia.
E-mail: knets@latnet.lv

Valentina Krilova, *leading researcher, Dr.chem.,*
Riga Technical University, Biomaterials R&D Laboratory,
Address: Azenes str. 14/24, Riga, LV-1048, Latvia.
E-mail: v.krilova@inbox.lv

Liga Berzina-Cimdiņa, *assoc. professor, Dr.sc. ing.,*
Riga Technical University, Biomaterials R&D Laboratory.
Address: Azenes str. 14/24, Riga, LV-1048, Latvia.
E-mail: liga@ktf.rtu.lv

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Introduction

Acrylic bone cements are widely used in bone restorative and replacement surgery. The most of commercially available bone cements are based upon poly(methylmethacrylate)-methylmethacrylate [P(MMA)-MMA] system and have linear polymer structure. These cements are used for many years with good clinical results. Nevertheless, some well-known properties of the cements are not satisfactory, mainly, high polymerization peak temperature and poor compatibility with bone. The temperature shock is considered to be the reason of surrounding tissues damage but weak adhesion to the bone may cause the aseptic loosening of the implant.

Several attempts have been done to improve biocompatibility of bone cements including the introduction of biodegradable additives; chitosan being among them [1].

Chitosan is N-deacetylated chitin and has some amount of remaining acetamido groups. It is a linear mucopolysaccharide, having β-(1-4)-D-glucosamine and N-acetyl- β-(1-4)-D-glucosamine units. Chitosan has been proposed for the development of different materials for biomedical applications [2, 3].

To get bone cements having better setting parameters acrylic bone cements (ABC) on the base of poly(MMA-co-hexylacrylate)-ethylmethacrylate-triethyleneglycol dimethacrylate [P(MMA-HA)-EM-TEGDMA] system have been developed in our laboratory [4, 5].

The present study concerns the modification of the cement by biodegradable additives-biopolymers chitosan and chitin. The last is used for comparison with chitosan taking into account the fact that commercial chitosan contains different amount of N-acetylated glucosamine units.

Materials and Methods

MMA, HA and EM were purified by vacuum distillation; TEGDMA, chitosan (middle-viscous, from crab shells,) and other reagents were used as received.

P(MMA-HA) copolymers were synthesized by suspension polymerization.

Chitin was isolated from shrimp exoskeleton by treatment with alkaline solution and washing with water.

To prepare bone cement specimens solid and liquid phases were mixed in proportion 1g:0.50ml for cement without additive, 1g:0.52ml for cement with 10% of chitosan or chitin and 1g:0.55ml for cement with 20% of chitosan or chitin in solid phase.

Setting parameters were measured mixing 1g of cement solid phase and corresponding amount of liquid one. The polymerization temperature was measured using Checktemp 1 (*HANNA Instruments*), resolution 0.1^{o}C, accuracy ±0.3^{o}C.

The mechanical properties were evaluated using INSTRON. The ultimate flexural strength values were found from four-point tests. Bone cement specimens were formed as rectangular bars and stored during 6 days in 0.01M phosphate buffer solution containing 0.14M NaCl and having pH 7.4.

Water uptake was measured after storing in the same buffer solution.

Results

Acrylic bone cement setting process is radical polymerization reaction which takes place in the presence of dissolved and nondissolved (co)polymer. In P(MMA-HA)-EM-TEGDMA system the polymer dissolution degree depends on HA content in copolymer. Polymer dissolution degree, in its turn, influences autoacceleration stage which is the most important stage of acrylic monomer(s) polymerization. As experiments showed the most appropriate content of HA in MMA-HA copolymer is 5-10%. FTIR spectra have been used to evaluate the content of residual vinyl groups in bone cements. The absorbance at ~1640 cm^{-1} represents valence vibration of conjugated double bond. This absorbance is not large, especially for bone cement formed from copolymer having 7% of HA (Fig.1). This formulation has been used in our further experiments.

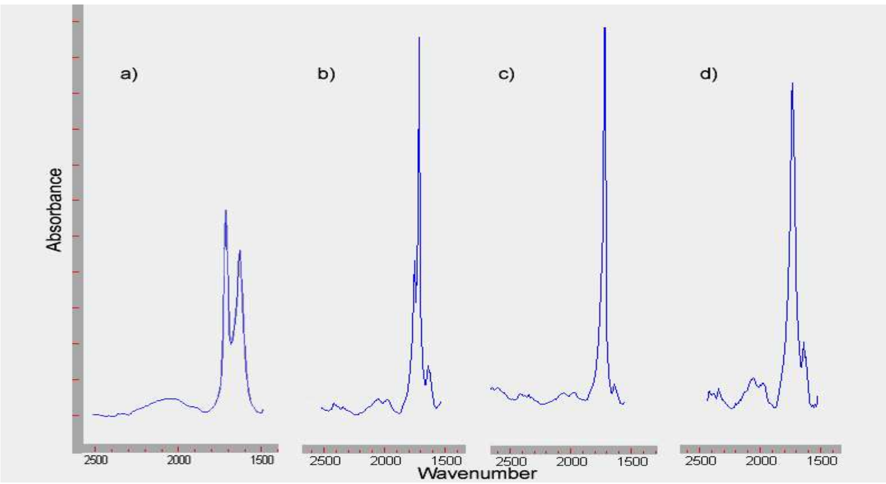


Fig.1 *FTIR spectra in diapason 1500-2500 cm^{-1} of: a) TEGDMA; b-d) ABC: HA content in solid phase: b) 5%; c) 7%; d) 10%*

The introduction of 10% and 20% of chitosan or chitin into bone cement solid phase influences little setting parameters of bone cement, however, some increase of polymerization peak temperature can be noticed (Fig.2).

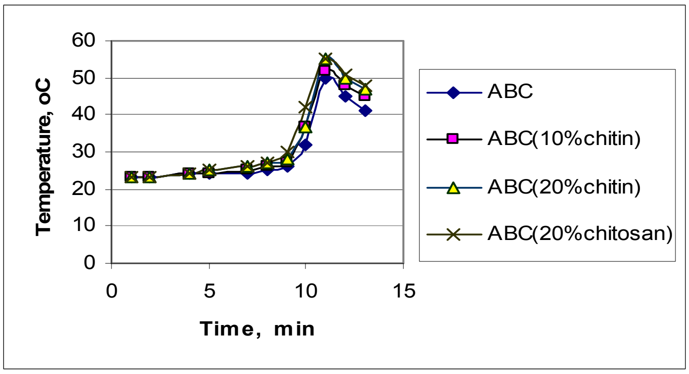


Fig.2. *Temperature profiles.*

Chitosan and chitin introduction into bone cement solid phase causes water uptake increase which is connected with hydrophilic character of the additives (Fig.3).

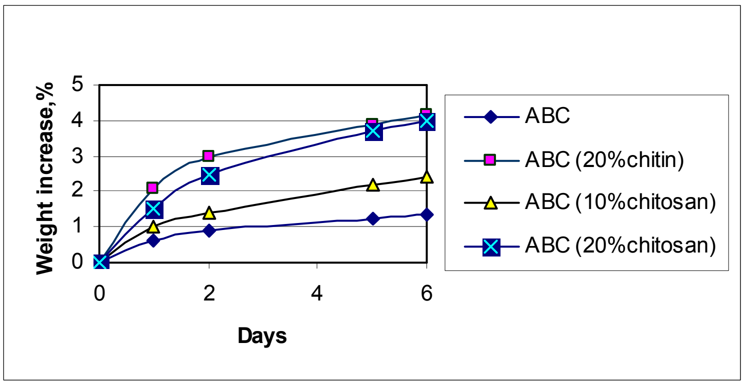
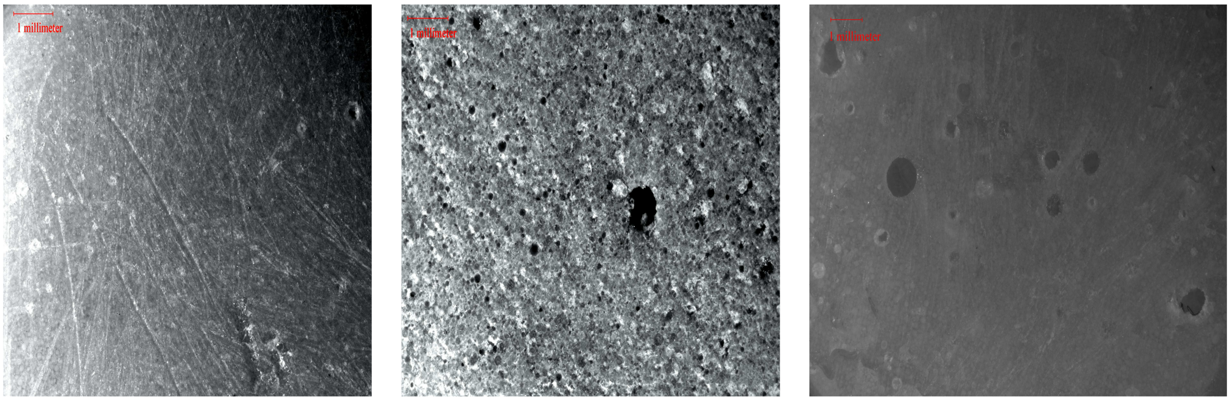


Fig.3. *Water uptake.*

Water uptake increase is desirable phenomenon for bone cement biocompatibility. Also the enhanced physical heterogeneity of bone cement surface is favorable. Pores existence can be noticed in the cement modified by chitosan and chitin introduction (Fig.4).



ABC | ABC(20% chitin in solid phase) | ABC(20% chitosan in solid phase)

Fig.4. *Surface of bone cements (magnification 10x)*

Factors which are favorable for better biocompatibility might cause decrease of bone cement mechanical strength. However, mechanical tests showed that chitosan and chitin introduction in studied amount did not cause large flexural strength decrease. Ultimate strength of bone cement specimens containing 20% of chitosan or chitin in solid phase has satisfactory values (Fig.5).

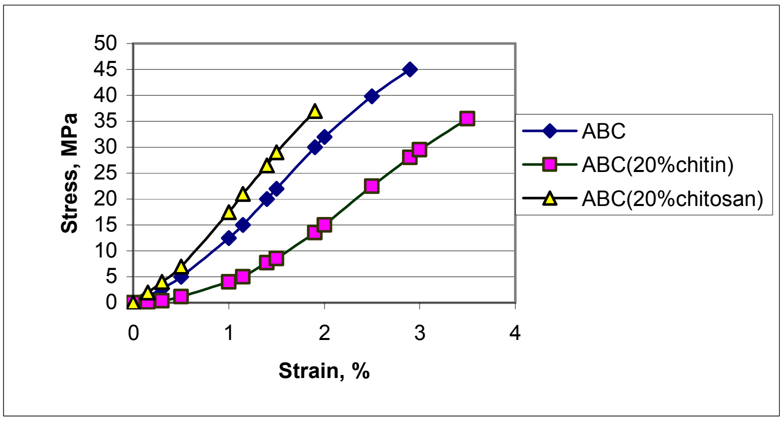


Fig.5. *Stress-strain characteristics (flexural test)*

The introduction of 20% chitosan into solid phase of bone cement does not influence practically the compressive strength of the cement (Fig.6), while the introduction of chitin decreases the value of strength in uniaxial compression.

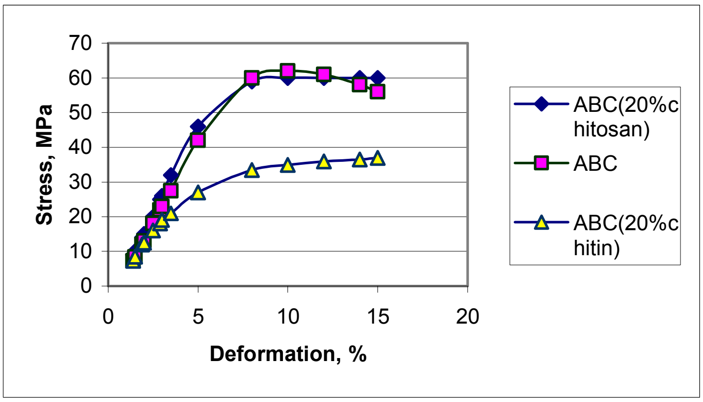


Fig.6. Stress-deformation relationship in uniaxial compression

Also tangent modulus of bone cement with chitin additive is much less than the modulus of bone cement modified with chitosan (Table).

Table

Mechanical parameters of bone cements*

Bone cement	Flexural tests		Uniaxial pressure	
	Ultimate stress, MPa	Modulus**, MPa	Ultimate stress, MPa	Modulus, *** MPa
ABC	47.65±6.63	1576±33.5	65.79±10.93	735.2±89.4
ABC(20% of chitin)	33.45±5.06	951.2±212.8	37.54±0.19	499.9±133.3
ABC(20% of chitosan)	40.11±5.60	1679±69.0	63.70±14.03	965.3±190.7

* - mean±STD;
**- between stresses (9-10) MPa
*** - between stresses (10-20) MPa

Conclusions

The introduction of 10% and 20% of biodegradable additives chitosan and chitin into solid phase of acrylic bone cement on the base of P(MMA-HA)-EM-TEGDMA influences little the cement setting parameters.
Water uptake increase, larger heterogeneity of bone cement surface, and the nature of additives might facilitate bone cement biocompatibility.
Taking into account comparatively small decrease of bone cement flexural ultimate strength and ultimate stress in uniaxial compression the bone cement modified with chitosan can be regarded as promising material for further investigation.

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Vītinš V., Knets** I., **Krilova V., Bērziņa-Cimdiņa L**. **Šķērssaišu saturošs akrila kaulu cements ar biodegradējošām piedevām.

Lai paaugstinātu 3-D polimēra struktūras kaula cementa biosaderību, kaulu cements uz poli(MMA-heksilakrilāts)-etilmetakrilāts-trietilēnglikoldimetakrilāta bāzes tika modificēts ar biodegradējošām piedevām - hitozānu un no garneļu čaumalām izdalītu hitīnu. Parādīts, ka norādīto piedevu ievadīšana cementa cietā fāzē izpētītā daudzumā maz ietekmē cementa sacietēšanas temperatūras profilu, bet izraisa ūdens absorbcijas un cementa virsmas heteroģenitātes palielināšanu. Hitozāna ievadīšana 20% daudzumā cietā fāzē praktiski neietekmē cementa stiprību liecē un aksiālā spiedē, bet hitīna ievadīšana 20% daudzumā izraisa graujošā sprieguma un moduļu lielumu samazināšanu abos testos.

Vitins V., Knets** I.,**.Krilova V., Berzina-Cimdina L. Cross-linked acrylic bone cement with biodegradable additives.

In order to enhance of 3-D polymer structure bone cement biocompatibility, the cement on the base of poly(MMA-hexylacrylate)-ethylmethacrylate-triethyleneglycol dimethacrylate has been modified by the introduction of biodegradable additives. Chitosan and isolated from shrimp exoskeleton chitin were introduced into cement solid phase. The introduction of mentioned additives in studied concentration influences little the temperature profile of cement setting, but increases water uptake and heterogeneity of the cement surface. The introduction of 20% chitosan into cement solid phase practically does not influence bone cement flexural strength and strength in uniaxial compression, but 20% chitin introduction arises the decrease of bone cement ultimate stress and modulus both in flexural tests and uniaxial pressure.

Витыньш В., Кнетс И., Крылова В., Берзиня-Цимдыня Л. Поперечносшитый костный цемент с биодеградирующими добавками.

С целью повышения биосовместимости костного цемента 3-D полимерной структуры, цемент на основе системы поли(ММА-гексилакрилат)-этилметакрилат-триэтиленгликольдиметакрилат модифицирован введением в твёрдую фазу биодеградирующих добавок - хитозана и выделенного из панциря креветок хитина. Показано, что введение в твёрдую фазу костного цемента указанных добавок в изученных количествах мало влияет на температурные профили затвердевания цемента, но вызывает увеличение поглощения воды и гетерогенности поверхности цемента. Введение 20% хитозана в твёрдую фазу цемента практически не влияет на прочность цемента на изгиб и сжатие, в то время как введение 20% хитина вызывает снижение величин разрушающего напряжения и модулей в обоих тестах.