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Acrylic Bone Cements Modified with Starch

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Abstract: **The successful result of restorative and replacement surgical operation depends significantly on properties of used bone cement. Acrylic bone cements are usually based on methylmethacrylate polymer, while monomer polymerization begins after mixing of components in mixing device and terminates in living tissue. Polymerization of methylmethacrylate is exothermic process, and temperature increase might cause tissue necrosis with concomitant implant aseptic loosening. Developed non-ionogenic and containing carboxylic groups of acrylic acid bone cements on the base of poly(methylmethacrylate-2-ethylhexylmethacrylate) – ethylmethacrylate- triethyleneglycol dimethacrylate system have appropriate setting parameters. The influence of polysaccharide nature additive introduction on main properties of developed bone cements has been studied. Starch was used as biocompatible and biodegradable component. The introduction of 20% starch into solid phase of bone cements aroused the change of setting profiles: polymerization peak temperature decreased and setting time increased. The mechanical properties of bone cements determined by pour-point bending and uniaxial compression tests were not worsened by starch introduction. The morphology of fracture of bone cements specimens was studied using electron microscopy. The data obtained testify that bone cements modification with starch additive is perspective for further achieving of bone tissue regeneration.**

Keywords: **bone cement, starch, setting properties, mechanical properties**

I. INTRODUCTION

Bone cement properties define greatly the successful result of bone restorative and replacement surgical operation.

Poly(methylmethacrylate) [P(MMA)] bone cements are formed by radical polymerization of methylmethacrylate (MMA); the process starts after mixing solid (powder) and liquid phases of cement composites. Polymerization takes place together with powder dissolution in monomer. The polymerization begins in mixing device, but the last phase of cement formation takes place in patient’s body.

MMA polymerization is exothermic process with temperature growth. This temperature shock is associated with risk of tissue thermal necrosis which can arise implant aseptic loosening [1, 2]. Overall, the thermal history of polymerization has considerable influence on the final properties of bone cement [3].

To achieve improvement of bone cement properties new cement compositions have been developed and also additives have been introduced into cements.

In comparison with P(MMA)-MMA cements the bone cement based on poly(ethylmethacrylate), hydroxyapatite powder and n-butylmethacrylate exhibits a lower exotherm. The interfacial temperature is lower than the threshold level for thermal tissue damage [3].

The lack of bioactivity of bone cement would be another factor which causes loosening between a bone and an implant. P(MMA) – MMA cements do not show bone-bonding ability, i.e. bioactivity [4]. Therefore efforts are made to develop bioactive bone cements.

Bioactive bone cements based on a paste-paste system consist of hydroxyapatite filler in a methacrylate matrix comprising urethane dimethacrylate and triethylene glycol dimethacrylate [5]. To improve the interface between inorganic filler and organic matrix the hydroxyapatite particles were treated using polyacrylic acid and γ-methacryloxypropyltrimethoxy silane. Polyacrylic acid surface treatment was found to be more effective in improving the interface, and the cement maintained mechanical properties after immersion in SBF [5].

Bone cement on the base of P(MMA)-polymethylacrylate/P(MMA) blend has been modified with resorbable biooligomer based on an amino acid trans-4-hydroxy-L-proline. The results suggest the decrease of mechanical properties of modified bone cement stored in wet conditions, while there was pores formation in the bone cement structure [6].

Biopolymers are an important source of materials with high chemical versatility and with high potential to be used in a range of biomedical application. Many of them are readily available. Natural based materials are also usually biocompatible and non-cytotoxic due to their similarity with living tissues [7].

Polysaccharides (starch, alginate, chitosan) have been proposed for different biomedical uses. These biopolymers are clearly biocompatible and do not lead to any inflammatory response. Moreover they are totally biodegradable [7].

Starch microspheres have been used as drug delivery carriers in tissue engineering applications [8]. The developed system has potential use for loading of growth factors for improving bone regeneration [8].

The aim of present study is to evaluate the results of bone cement modification with material of polysaccharide nature. The introduction of starch additive has been done into developed bone cements:

- on the base of poly(methylmethacrylate-2-ethylhexylmethacrylate)-ethylmethacrylate-triethyleneglycol dimethacrylate [P(MMA-EHMA)-EMA-TEGDMA],
- functionalized with carboxylic groups, i.e., on the base of (methylmethacrylate-2-ethylhexylmethacrylate)-ethylmethacrylate-acrylic acid -triethyleneglycol dimethacrylate [P(MMA-EHMA)-EMA-AA-TEGDMA].

The influence of additive introduction into cements solid phase on their setting parameters, mechanical properties, and water absorption has been under consideration.

II. MATERIALS AND METHODS

EMA and AA were purified by vacuum distillation; MMA, TEGDMA, EHMA (all ALDRICH) and other reagents were used as received.

P(MMA-EHMA) copolymer was synthesized by suspension polymerization. EHMA content in P(MMA-EHMA) was 8%. The content of cross-linking agent TEGDMA in liquid phase was 8% for P(MMA-EHMA)-EMA-TEGDMA bone cement (ABC-8) and 6% for P(MMA-EHMA)-EMA-AA-TEGDMA cement (ABC-6-3A). Spherical beads of copolymer were washed, dried and sieved, and fraction less than 100 µm being collected as working fraction. Mean diameter of copolymer beads was ~ 60 µm.

The content of initiator of polymerization benzoyl peroxide was 1% in solid phase.

The content of activator N,N-dimethyl-p-toluidine was 1% in liquid phase. Hydroquinone was added to liquid phase for stabilization during storage.

To prepare bone cement specimens solid and liquid phases were mixed in proportion 2g:1ml. 20% of starch was introduced into solid phase instead of the same amount of copolymer powder. Potatoes starch powder was used without treatment.

Setting parameters were measured in polyethylene mould using Checktemp 1 (HANNA Instruments), resolution 0.1^0C, accuracy $\pm 0.3^0$C. Setting time was defined as time corresponding to temperature $T_{set}=(T_{max}+T_{amb})/2$, where T_{max} – polymerization peak temperature, ^oC; T_{amb} – ambient temperature, ^oC [1].

The mechanical tests (in bending and in compression) were carried out using INSTRON 4301. Using four-point flexural tests and uniaxial compression the ultimate strength and elastic modulus of material were found from stress - strain relationship. Bone cement specimens were formed as rectangular bars for bending tests and as cylinders for tests in compression. Before testing in bending specimens were stored during 6 days in 0.01M phosphate buffer solution containing 0.14 M NaCl and having pH 7.3. Tests in compression were done after storing samples for 24 h in dry condition [1].

Bone cement morphology in fracture was studied using Tescan Mira//LMU Schottky type electron microscope (SEM).

III. RESULTS

Polymerization reaction of acrylic monomers is exothermic process with expressed auto acceleration stage; therefore acrylic bone cement setting is accompanied by temperature growth, the level of which depends not only on polymerization enthalpy but also on heat capacity of the system. During cement setting heat dissipation into surrounding medium takes place, also heat absorption by polymerizing mixture itself is consequential factor. Setting process of acrylic bone cement on the base of P(MMA-EHMA)-EMA-TEGDMA is accompanied by less temperature growth as compared with P(MMA)-MMA cements, despite the presence of cross-linking agent TEGDMA.

To get a composite with carboxylic groups, the introduction of acrylic acid into liquid phase of bone cement has been done. This might provide bioactivity of bone cement due to possibility to attach polar surroundings.

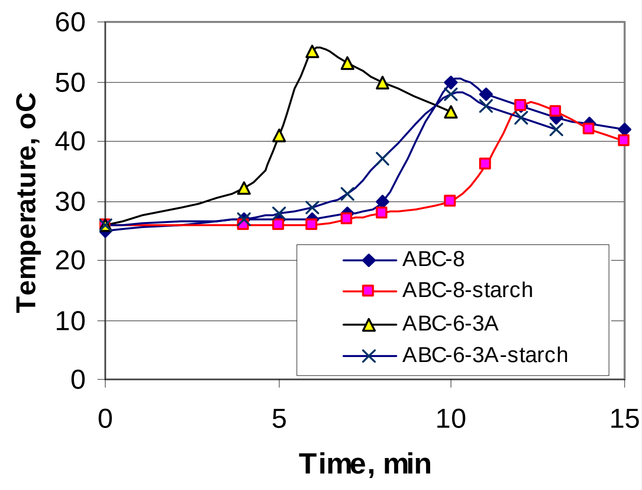

Fig. 1. Setting profiles of modified with starch and non-modified bone cements on the base of P(MMA-EHMA)-EMA-TEGDMA (ABC-8) and P(MMA-EHMA)-EMA-AA-TEGDMA (ABC-6-3A)

The introduction of AA into monomer mixture generated the increased polymerization peak temperature and the decreased setting time (Fig.1). Experiments showed that the introduction of only 3 percents of AA led to intensification of polymerization process. This phenomenon might have positive effect on the degree of monomer(s) conversion.

Bone cement modification with starch may be favorable for the cement biocompatibility increase as well as for further additive biodegradation and substitution with bone tissue.

Substitution of 20% of P(MMA-EHMA) dispersion by the same amount of starch caused the change of bone cement setting profiles (Fig.1). Polymerization peak temperature of modified cement ABC-8 was lower but setting time was longer in comparison with non modified cement (9 min and 11min, accordingly).

The additive introduction into P(MMA-EHMA)-EMA-AA-TEGDMA cement aroused the change in setting profiles analogous to change in P(MMA-EHMA)-EMA-TEGDMA cement (Fig.1), namely peak temperature decrease and setting time increase (5 min and 8 min, accordingly). Noticed setting process change may be connected with retention of polymerization process as well as with heat capacity change in the system caused by starch introduction.

Bone cement setting process practically leads to rather heterogenic structure formation.

Non solvated (co)polymer beads and some pores usually exist in all specimens. Additive introduction increases heterogeneity of bone cement fracture (Fig.2, Fig.3). Despite of smooth surface of starch grains the contact between additive and polymer material is rather close.

Surface properties and the nature of additive influence their interconnection with copolymer material of formed cement. All these define mechanical properties of formed samples. Mechanical tests in bending and in compression showed that starch introduction had insignificant influence on ultimate stresses of materials, but modulus of elasticity increased about 1.4 times in compression and practically was unchanged in bending (Table 1).

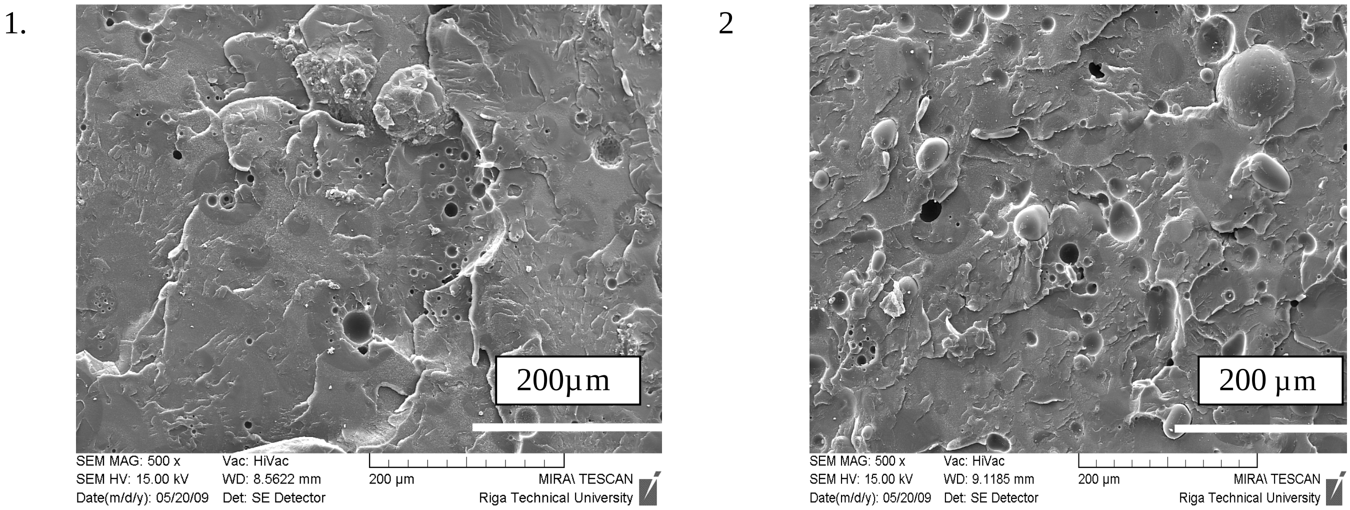

Fig.2. SEM image of bone cements fracture: 1-ABC-8; 2-ABC-8-starch

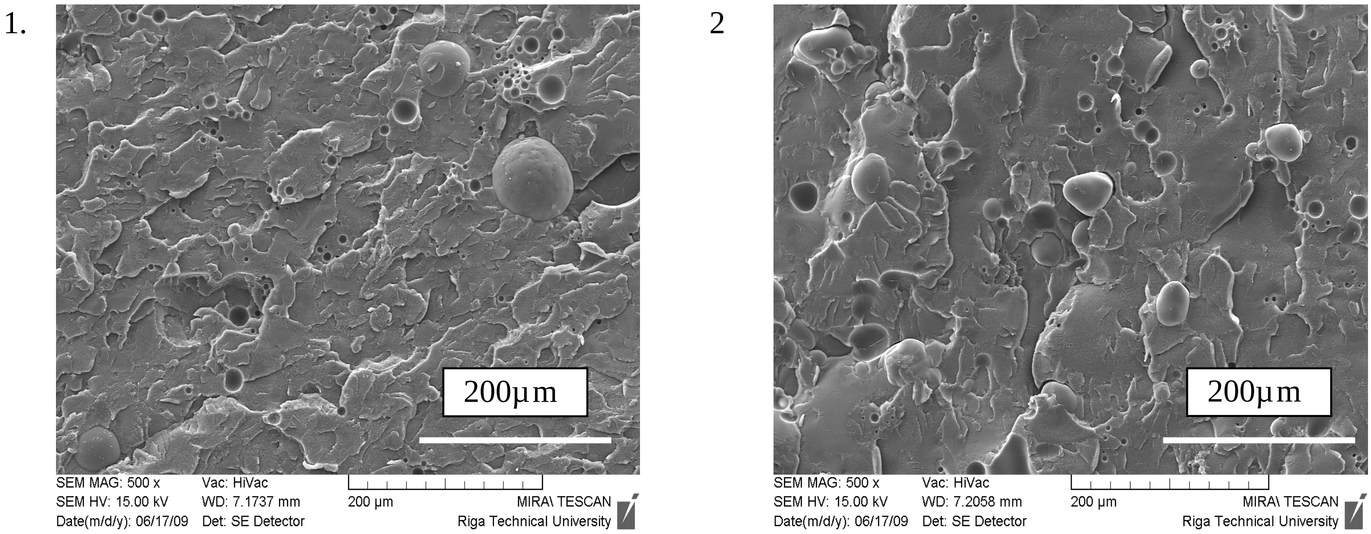

Fig.3. SEM image of bone cements fracture: 1-ABC-6-3A; 2-ABC-6-3A-starch

TABLE 1

MECHANICAL PROPERTIES OF BONE CEMENTS FROM BENDING AND COMPRESSION TESTS*

Bone cement	Flexural tests		Uniaxial pressure	
	Ultimate stress, MPa	Modulus of elasticity**, MPa	Ultimate stress, MPa	Modulus of elasticity**, MPa
ABC-8	54.99±10.61	1670±189	75.16±1.53	877±17
ABC-8 -starch	49.90±2.05	1888±176	83.63±11.27	1195±149
ABC-6-3A	56.85±2.10	1612±500	106.01±1.00	800±298
ABC-6-3A-starch	62.03±10.12	1575±13	104.30±3.20	1152±18

* - mean ± STD
**- between stresses (10-20) Mpa

One of bone cement properties dealing with its biocompatibility is the cement hydrophility. Biodegradation of additives and bone tissue formation cannot take place without the close contact with fluids. Starch from potatoes contains highly hydrophilic amilose and amilopectin components.

The introduction of starch led to essential increase of water uptake by bone cements (Fig.4).

Polysaccharide nature additive (starch) has been introduced into bone cement P(MMA-EHMA)-EMA-TEGDMA and having carboxylic groups P(MMA-EHMA)-EMA-AA-TEGDMA cement. The introduction of 20% of this additive influenced the setting parameters of the cements: polymerization peak temperature decreased and setting time increased.

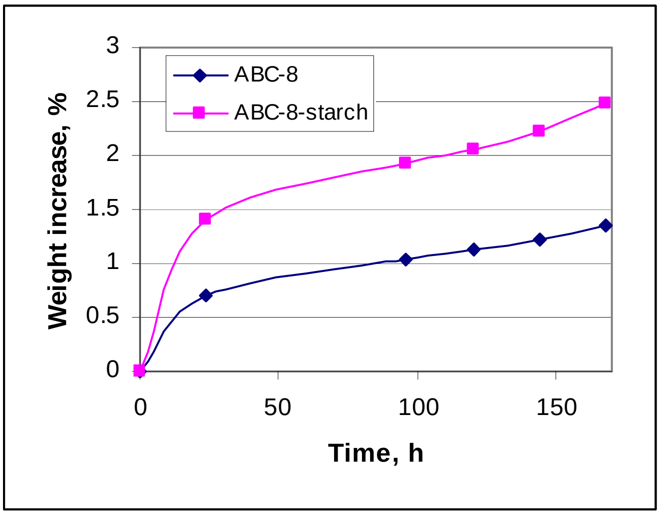

Fig.4. Water uptake by bone cements

IV CONCLUSIONS

The modification of developed bone cements with starch did not worsen mechanical parameters of the cements determined by four-point bending tests and uniaxial compression.

Hydrophility of bone cements increased with the introduction of starch additive.

The data show that bone cement modification with biocompatible and biodegradable starch is promising procedure for developing cements with tendency of bone cells ingrowth.

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Valentīna Krilova, Visvaldis Vītiņš. Ar cieti modificietie akrila kaulu cementi.
Atjaunojošās un aizvietojošās ķirurģiskās operācijas sekmīgs rezultāts lielā mērā atkarīgs no kaulu cementa īpašībām. Parasti akrila kaulu cementu pamatā ir metilmetakrilāta polimērs. Monomēra polimerizācija sākas samaisot komponentus maisīšanas ierīcē un noslēdzas dzīvajos audos. Metilmetakrilāta polimerizācija ir ekzotermisks process, un temperatūras paaugstināšana var izraisīt audu nekrozi ar tālāko implanta fiksācijas atslābināšanu. Izstrādātiem nejonogēnam un akrilskābes karboksilgrupu saturošam kaulu cementiem uz poli(metilmetakrilāta-2-etilheksilmetakrilāta) – etilmetakrilāta-trietilēnglikoldimetakrilāta bāzes piemīt apmierinoši sacietēšanas parametri. Izpētīta biosaderīgas un biodegradējamas piedevas (cietes) ietekme uz izstrādāto kaulu cementu pamatīpašībām. 20% cietes ievadīšana kaulu cementu cietā fāzē izraisa izmaiņas sacietēšanas profilā: polimerizācijas maksimālas temperatūras samazināšanu un sacietēšanas laika palielināšanu. Kaulu cementu mehāniskās īpašības nepasliktinās ar cietes piedevas ievadīšanu. Mehāniskās īpašības tika noteiktas no četrpunktu lieces un vienass spiedes testiem. Cementu paraugu morfoloģija pētīta lietojot elektronu mikroskopiju. Iegūtie dati liecina par kaulu cementu modifikācijas perspektivitāti, lietojot kā piedevu cieti ar nolūku veicināt tālāku kaulaudu reģenerāciju.

Валентина Крылова, Высвалдис Витыньш. Модифицированные крахмалом акриловые костные цементы.
Успешный результат восстановительной и замещающей хирургической операции в значительной степени определяют свойства костного цемента. Акриловые костные цементы обычно представляют собой полимер метилметакрилата, причём полимеризация мономера начинается при смешении компонентов в смесительном устройстве, а заканчивается в живой ткани. Полимеризация метилметакрилата – экзотермический процесс, и повышение температуры может привести к некрозу ткани с последующим ослаблением фиксации импланта. Разработанные костные цементы - неионогенный на основе системы поли(метилметакрилат-2-этилгексилметакрилат) – этилметакрилат-триэтиленгликольдиметакрилат, а также содержащий карбоксильные группы акриловой кислоты в этой системе – имеют приемлемые параметры затвердевания. Изучено влияние введения биосовместимой и биодеградируемой добавки крахмала на основные свойства разработанных костных цементов. Введение 20% крахмала в твёрдую фазу костных цементов вызывает изменение профилей затвердевания: снижение максимальной температуры полимеризации и возрастание времени затвердевания. Механические свойства костных цементов, определённые в тестах на четырёхточечный изгиб и одноосное сжатие, не ухудшаются при введении добавки крахмала. Морфология разломов образцов цементов изучена с помощью электронной микроскопии. Полученные данные свидетельствуют о перспективности модификации костных цементов добавкой крахмала с целью достижения последующей регенерации костной ткани.