Examination of the suitability of α-tocopherol as a stabilizer for ultra-high molecular weight polyethylene used for articulating surfaces in joint endoprostheses

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The lifetime of articulating surfaces in joint endoprostheses made of ultra-high molecular weight polyethylene (UHMW-PE), especially of UHMW-PE-cups of hip-endoprostheses, is usually limited to 10–15 years due to material failure as a result of oxidation of the UHMW-PE *in vivo*. In this study the suitability of the natural antioxidant α-tocopherol (vitamin E) as a stabilizer for UHMW-PE in these applications was investigated. Specimens with 0.1%, 0.2%, 0.4% and 0.8% w/w α-tocopherol as well as unstabilized samples were sintered and sterilized with γ-rays at 25 kGy in accordance with standard processing methods of cups for total hip-endoprostheses. These specimens were aged in pure oxygen at 70 °C and 5 bar as well as in aqueous H_2O_2 at 50 °C. The degree of oxidation was observed by means of FTIR-spectroscopy, DSC analysis and mechanical testing. The FTIR-measurements showed that α-tocopherol can prolong the lifetime of UHMW-PE in an oxidative environment by a factor of more than 2.5. In the mechanical tests no embrittlement could be observed with the stabilized samples. A comparison with the standard antioxidant system Irganox® 1010/Irgafos® 168 (Ciba-Geigy, Switzerland) was carried out and revealed that α-tocopherol can even exceed the stabilization effect of this widely-used antioxidant system.

1. Introduction

Ultra-high molecular weight polyethylene (UHMW-PE) has been used successfully for articulating surfaces in joint endoprostheses, especially for cups of total hip-endoprostheses, for more than 30 years. The lifetime of the cups has been increased over the last years and now usually reaches 10–15 years, but such a long lifetime is not always achieved due to material failure [1].

Previous examinations have proven UHMW-PE to be oxidized *in vivo* [2–5], which leads to an increased wear-rate and in consequence to an high amount of PE-debris in the surroundings of the prosthesis [6] followed by an inflammation of adjacent tissue, often accompanied by osteolysis [7]. As a result of this inflammation, the prosthesis must be retrieved immediately in most cases.

The oxidation process is initiated during processing and sterilization of the cups and continues *in vivo*. Free radicals are produced due to bond scission especially in the sterilization step with γ-rays or are already present in the human body such as hydroxy-radicals [8, 9]. In the presence of oxygen, the O_2 molecules add to these radicals and form peroxides, which accelerate the oxidation and lead to a chain-scission of the polyethylene-backbone [4, 10–14]. As a result of this break, the molecular mass is lowered. Due to the higher mobility of the shorter PE-chains formed by chain-scission, the cristallinity as well as the density increases [5] which causes an embrittlement of the material [3]. All this leads to an enhanced formation of PE-debris by the articulating action of the joint [15].

In fact, the oxidative degradation of polyolefins is a well-known technical problem and is usually inhibited by adding stabilizers to the polymer, e.g. hindered phenols as Irganox® 1010. For applications *in vivo*, the use of any of the standard antioxidants is not permitted due to the toxicity of these synthetic substances.

Closer examination of the human body reveals that some vitamins, especially the fat-soluble α-tocopherol (vitamin E), show an antioxidant effect. A suggestion was made by B. Doležel and L. Adamírová [16], to use α-tocopherol as a non-toxic, natural antioxidant for polyolefins against thermal oxidation during the manufacture of the material or against photo-oxidation of the material under natural environmental conditions. Up to now this suggestion was not followed by the producers of joint endoprostheses; in consequence all present hip-cups

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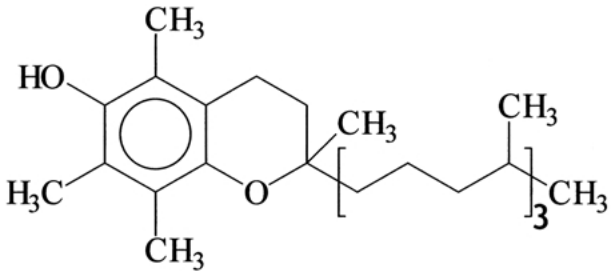

Figure 1 Chemical structure of α-tocopherol.

made of UHMW-PE consist of neat polyethylene without any stabilizers (according to ISO 5834 Part 1 and 2).

In the human body the α-tocopherol acts as a scavenger of free radicals, which can directly or indirectly initiate ($^1O_2, O_2^{\bullet}$, $HO^{\bullet}$, etc.) or propagate (lipid peroxyl radicals) the oxidation of LDLs (low-density lipoproteins) [17]. When regarding the chemical structure of α-tocopherol (Fig. 1), which has a phenolic group situated para to the oxygen of the chroman ring [18], the stabilization mechanism becomes quite obvious and is the same as with standard hindered phenols: the α-tocopherol reacts with radicals to give the stable tocopheroxyl radical (proton-transfer). The final oxidation product *in vivo* is the α-tocopheryl quinone [19], while diastereoisomers of dimers and trimers as well as aldehydes were found in α-tocopherol stabilized LDPE after extrusion [20].

In this study, UHMW-PE samples were stabilized with different concentrations of α-tocopherol and aged *in vitro* by means of aqueous H_2O_2 at 50 °C and by O_2 under 5 bar and 70 °C [21]. The test specimens were processed in the same way as standard hip-cups. The process of oxidation of the stabilized UHMW-PE was then observed using spectral, thermal and mechanical methods and compared to unstabilized specimens as well as to specimens stabilized with the standard combination of the antioxidants Irganox® 1010/ Irgafos® 168.

2. Materials and methods

2.1. Preparation and processing of specimens

UHMW-PE was Hostalen GUR 1020 from Hoechst AG (now TICONA AG), which fulfills the requirements of ISO 5834 Part 1 and 2 (Implants for surgery – UHMW-PE powder and molded forms) and was obtained as a gift sample from the production site in Oberhausen, Germany. DL-α-Tocopherol was a gift sample of Hoffmann-La Roche (Grenzach-Wyhlen, Germany). α-Tocopherol is a brownish oil with a high viscosity, thus it was dissolved in ethanol (with a concentration of 50 g/l) and mixed into the UHMW-PE-powder drop by drop in a screw-cone mixer (Nauta-Vrieco). The ethanol was then evaporated in a vacuum-dryer at 50 °C for 6 h. Four different blends of UHMW-PE with 0.1%, 0.2%, 0.4% and 0.8% w/w-α-tocopherol were prepared. These four blends and neat UHMW-PE were each sintered to disks (diameter = 600 mm, thickness = 60 mm) at 220 °C and 35 bar for 7 h in an industrial facility usually used for the production of running surfaces of skis at Isosport GmbH (Eisenstadt, Austria).

One blend of UHMW-PE and 0.05% powdery antioxidant Irganox® 1010 (3-(3,5ditert.butyl-4-hydroxyphenyl)-propionate, Ciba-Geigy) and 0.05% powdery antioxidant Irgafos® 168 (tris-(2,4-di-tert.butylphenyl)-phosphite, Ciba-Geigy) were produced without any precautions in the same mixing device.

HPLC studies were carried out to determine the homogeneity of the α-tocopherol distribution. The α-tocopherol concentration of test samples, each taken from different locations of the disk, differed only by about ± 2% from the desired concentration.

For the FTIR-spectrometry, blocks with the dimension 20 mm × 20 mm × 40 mm were cut out of the middle of the disk. These blocks were washed and sterilized with γ-rays (25 kGy) in inert atmosphere by Sulzer Orthopaedic AG (Winterthur, Switzerland) according to the standard procedure for artificial hip-cups. Finally, microtom cuts with a thickness of 0.3 mm were prepared out of the blocks.

For the determination of the onset-temperature of thermal oxidation in the DSC, plates with the dimension 150 mm × 60 mm × 1 mm were milled out of the middle of the disk and washed and sterilized in the same way as above. After aging, small pieces of about 10 mg were cut out of the plates for DSC analysis.

The test specimens for the comparison tests of different stabilized samples (cf. Fig. 5 and Fig. 6) were sterilized with γ-rays in air atmosphere instead of inert atmosphere. For the mechanical tests, unsterilized specimens were tested before aging in order to see the influence of the irradiation on the material.

2.2. Accelerated aging

For the mechanical testings, accelerated aging was applied to the specimens by pure oxygen at 70 °C and 5 bar. For the evaluation of the onset-temperature and the FTIR-analysis, the specimens were stored in 1% and 5%, respectively, aqueous H_2O_2 at 50 °C with 0.04 mg/ml $FeCl_3$ as catalyst.

2.3. Fourier-transforming infrared spectroscopy (FTIR)

A Perkin Elmer FTIR 1600 spectrometer (resolution 4 cm^{-1}) was used to determine the Carbonyl (CO)-number according to DIN 53383. The CO-number is the ratio of the absorbance at 1718 cm^{-1} (carbonyl group) to the absorbance at 2020 cm^{-1} (C–H bond) and is a measure of the degree of oxidation of the material. The test films were placed directly in the mounting of the FTIR.

2.4. DSC-analysis

The onset temperature of oxidation was determined with a Perkin Elmer DSC 7 according to ISO 3146. The specimens were heated from room temperature to 180 °C in oxygen atmosphere at a heating rate of 100 °C per minute, kept at 180 °C for one minute to ensure a homogenous temperature distribution within the sample and then heated up to 300 °C at a heating rate of 10 °C per minute. The onset-temperature is the temperature when

the degradation of the test material due to oxidation is initiated. This exothermic reaction can be observed by means of DSC.

2.5. Mechanical testing

The tensile tests were carried out according to ISO 527 at a rate of elongation of 100 mm per minute, the impact tests according to ISO 11542. The specimens were milled out of the middle of the sintered discs, type 1B for the tensile test, double-notched samples for the impact test. The results are the mean values of five tests.

3. Results

3.1. Mechanical properties

Fig. 2 shows the results of the mechanical tests, giving the average values and the minimum/maximum-error bars. The values presented at negative storage time are obtained from unsterilized samples. All results show clearly the high degree of embrittlement of the unstabilized samples due to oxidation. After 60 h in pure oxygen at 70 °C and 5 bar, the modulus raises from 1000 to over 3000 N/mm^2 (Fig. 2A), the breaking elongation drops from 425% to nearly 0% (Fig. 2C) and in the impact testing the specimens broke before any testing was applied (Fig. 2D).

The mechanical properties of the stabilized samples stayed nearly constant over the entire aging time. Even after 120 h storage time, no drop of the values could be observed.

There is no remarkable difference in the stabilization effect between the samples stabilized with 0.1% and 0.8% α-tocopherol. The sample stabilized with 0.8% α-tocopherol shows a slight drop of the modulus and an increase of the breaking elongation and impact strength. At this concentration, the α-tocopherol acts similar to a softening agent.

The influence of the γ-irradiation (with a dose usually applied for sterilization) on the mechanical properties of the test material is rather insignificant except for the impact strength, which drops from 187 kJ/m^2 to 120 kJ/m^2 for the unstabilized sample. The stabilized samples also showed a drop of the impact strength after this irradiation with γ-rays, but the effect is much weaker than with the unstabilized sample.

3.2. FTIR-spectroscopy

The progress of oxidation in 5% aqueous H_2O_2 was observed with the help of FTIR-spectroscopy. Fig. 3 shows the Carbonyl (CO)-number of the differently stabilized specimens versus the storage time in H_2O_2. As expected, the stabilized samples are oxidized much slower than the unstabilized ones and the more α-tocopherol is added the better is the protection against oxygen. The time till the CO-number exceeded the value of two was evaluated to compare the stabilizing effect at different concentrations. The CO-number of two is a well-established limit applied in the film-processing industry to sort out damaged films made of PE-HD. The results are presented in Fig. 4. Adding 0.4% α-tocopherol to UHMW-PE raises the time till the CO-number exceeds 2 from approx. 230 h to 600 h. If such a prolongation of service life by a factor of almost 3 could be reached for UHMW-PE in hip-cups, it would cause a prolongation of the lifetime of hip-cups to approximately 30 years. Adding more α-tocopherol only results in a slight further increase of the stabilization effect, therefore it seems to

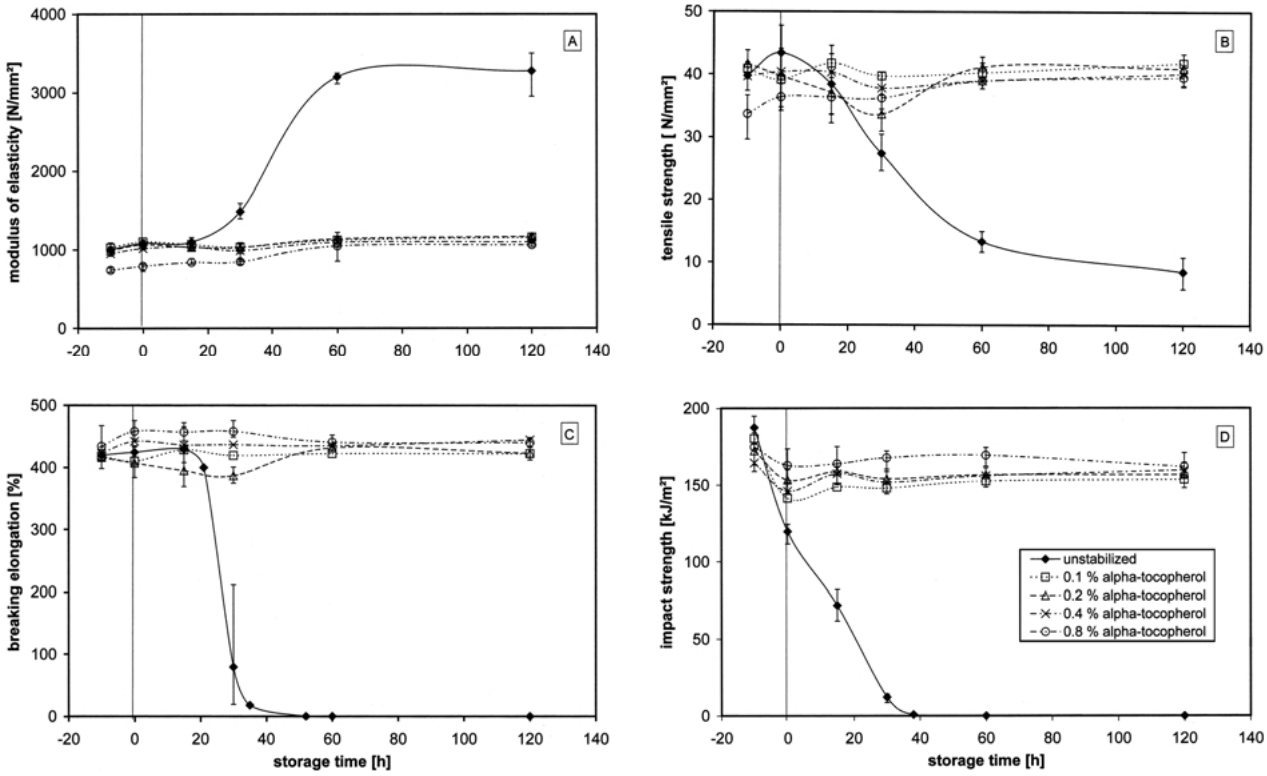

Figure 2 Modulus of elasticity (A), tensile strength (B), breaking elongation (C) and impact strength (D) as a function of the storage time in pure oxygen at 70 °C and 5 bar of differently stabilized UHMW-PE-specimens. Values at negative storage time were obtained from unsterilized samples.

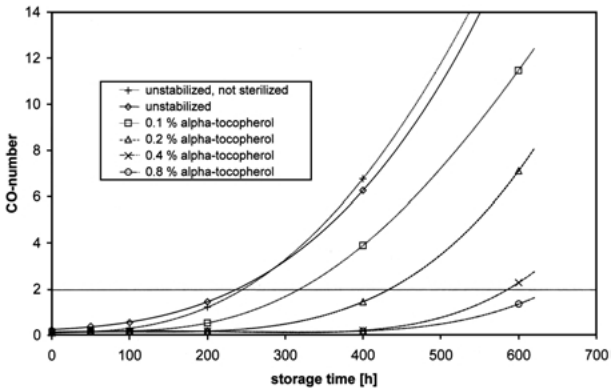

Figure 3 Carbonyl (CO)-number of differently stabilized UHMW-PE-specimens as a function of the storage time in 5% aqueous H_2O_2 at 50 °C.

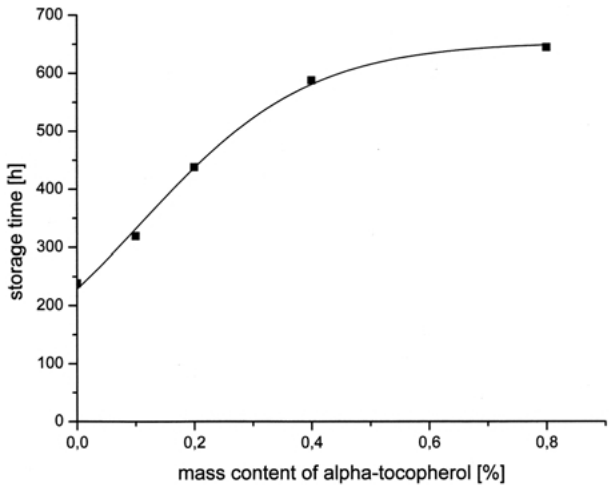

Figure 4 Storage time to reach values of the carbonyl (CO)-number of 2 versus mass content of α-tocopherol.

be useless to add more than 0.4% or 0.8% of α-tocopherol.

3.3. Comparison of different stabilizers

In order to compare the stabilizing effect of α-tocopherol with standard antioxidants, specimens with 0.05% and 0.2% α-tocopherol as well as with 0.05% Irganox® 1010/Irgafos® 168 were prepared and aged in 1% aqueous H_2O_2. The processing parameters were kept constant as described in Section 2.1 except that the samples were sterilized in oxygen instead of inert atmosphere. The progress of oxidation was again observed with FTIR-spectroscopy. Furthermore the onset-temperature was evaluated with DSC. The results are presented in Fig. 5 and Fig. 6.

Fig. 5 reveals that 0.2% α-tocopherol has an even better stabilization effect than the widely used combination of Irganox® 1010/Irgafos® 168, each with a mass content of 0.05%. Another interesting fact can be observed when regarding the CO-number of the samples before any aging: the unstabilized sample, irradiated in air, already showed an CO-number of 1.56, while the unstabilized sample, irradiated in inert atmosphere, shows an CO-number of 0.23 (Fig. 3) after irradiation. Hence the sterilization conditions have a great impact on the pre-damaging of the material. Thus manufacturers

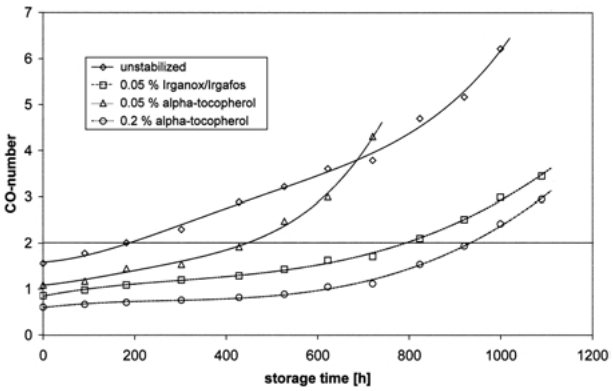

Figure 5 Comparison of different antioxidant systems: Carbonyl (CO)-number of differently stabilized UHMW-PE-specimens in air as a function of the storage time in 1% aqueous H_2O_2 at 50 °C.

should pay close attention to exclude any oxygen in the sterilization process.

The examination of the onset-temperature in the DSC leads to similar results (Fig. 6): α-tocopherol can easily stand up against Irganox® 1010/Irgafos® 168 as a stabilizer for UHMW-PE. At a concentration of 0.05%, the stabilizing effect of α-tocopherol and Irganox® 1010/Irgafos® 168 can be considered to be equal, while adding 0.2% α-tocopherol raises the onset-temperature for another 12 °C.

4. Conclusion

In this study the suitability of α-tocopherol as a stabilizer for UHMW-PE used for cups of hip-endoprostheses was investigated. All examinations showed that the natural antioxidant α-tocopherol can prolong the life-time of UHMW-PE crucially under oxidative conditions. No embrittlement, which would lead to an enhanced wear-rate of the material, could be observed with the stabilized samples. Compared to standard antioxidant-systems like Irganox® 1010/Irgafos® 168, α-tocopherol shows a comparable stabilizing effect.

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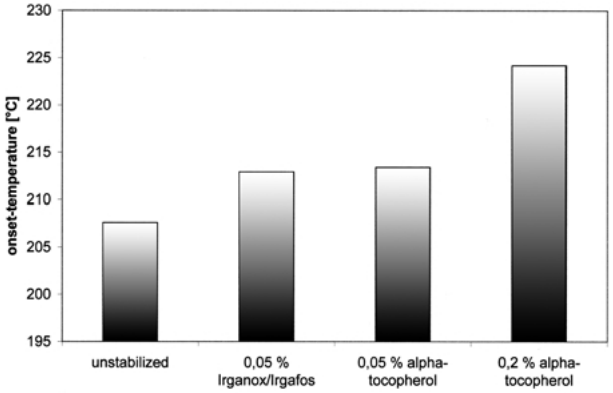

Figure 6 Onset-temperature of oxidation of UHMW-PE samples stabilized with different antioxidants.

References

1. R. M. ROSE and E. L. RADIN, *Biomat.* **11** (1990) 63.
2. M. GOLDMAN, R. GRONSKY, R. RANGANATHAN and L. PRUITT, *Polymer* **37** (1996) 2909.
3. P. EYERER, *Kunststoffe* **77** (1987) 617.
4. F. J. BUCHANAN, B. SIM and S. DOWNES, *Plast., Rub. and Comp. Proc. and Appl.* **27** (1998) 148.
5. E. S. GROOD, R. SHASTRI and C. N. HOPSON, *J. Biomed. Mat. Res.* **16** (1982) 399.
6. J. A. DAVIDSON and G. SCHWARTZ, *J. Biomed. Mat. Res.: Appl. Biomat.* **21** (1987) 261.
7. B. ZICAT, C. A. ENGH and E. GOKCEN, *J. Bone a. Joint Surg.* **77A** (1995) 432.
8. M. GOLDMAN, R. GRONSKY, G. LONG and L. PRUITT, *Poly. Deg. and Stab.* **62** (1998) 97.
9. M. DENG and S. W. SHALABY, *J. Appl. Polym. Sci.* **58** (1995) 2111.
10. J. L. HENRY, L. R. ASCENION and A. GARTON, *J. Polym. Sci.: Polym. Chem.* **30** (1992) 1693.
11. E. BRACH DEL PREYER, M. CROVA, L. COSTA, A. DALLERA, G. CAMINO and P. GALLINARO, *Biomat.* **17** (1996) 873.
12. L. COSTA, M. P. LUDA, L. TROSSARELLI, E. M. BRACH DEL PREVER, M. CROVA and P. GALLINARO, *ibid.* **19** (1998) 659.
13. *Idem.*, *ibid.* **19** (1998) 1371.
14. M. GOLDMAN, M. LEE, R. GRONSKY and L. PRUITT, *J. Biomed. Mat. Res.* **37** (1997) 43.
15. R. M. ROSE, E. V. GOLDFARB, E. ELLIS and A. N. CRUGNOLA, *J. Orthop. Res.* **2** (1984) 393.
16. B. DOLEŽEL and L. ADAMÍROVÁ, CS Pat. 221 403 (1981).
17. B. FREI, K. BRIVIBA and H. SIES in ''Natural Antioxidants in Human Health and Disease'' (Academic Press, San Diego, 1994) p. 107.
18. S. LAERMER in ''Proceedings of the ADDCON 95, World-wide Additive and Polymer Conference'', Basel, 1995.
19. R. CASANI in ''Kirk-Othmer, Encyclopedia of Chemical Technology'', Vol. 25, 4th ed. (John Wiley & Sons, New York, 1997) p. 256.
20. S. AL-MALAIKA, H. ASHLEY and S. ISSENHUTH, *J. Polym. Sci.* **32** (1994) 3099.
21. W. M. SANFORD and K. A. SAUM in ''Proceedings of the 41st Annual Meeting of the Orthopaedic Research Society'', Orlando, 1995.

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