Migration Stability of Antioxidant Containing Ultra High Molecular Weight Polyethylene at 75 and 115 kGy Sterilization Doses

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Purpose: The long term oxidative stability of Ultra High Molecular Weight Polyethylene (UHMWPE) is a very desirable for orthopedic bearing applications[1]. A post irradiation treatment (remelting) has been implemented to quench free radicals generated during gamma processing of UHMWPE, yielding the implant much less susceptible to oxidative degradation. An alternative to this approach would be the addition of an antioxidant (**AO**) into the UHMWPE. Incorporation of Vitamin E (Figure1) prior to gamma processing as well as after irradiation has been reported in the literature[2]. The procedure of doping UHMWPE (crosslinked) in Vitamin E (liquid at room temperature) followed by homogenization in inert gas increases the concerns about the migration and elution of Vitamin E during in-vivo use[3]. In this study, an **AO** pentaerythritol tetrakis [3-(3,5-di-tert-butyl-4-hydroxyphenyl) propionate] (Figure 2) was used to stabilize UHMWPE (**AO-Poly**). The AO is compounded with UHMWPE in the powder form, and the homogeneity of the powder mixture is confirmed prior to consolidation. Since AO is solid at room temperature, migration of the AO would not be an issue. This assumption was verified by extraction studies conducted after gamma processing AO-Poly at 75 and 115 kGy doses.

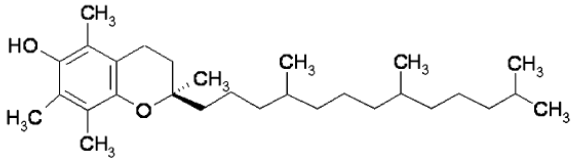

Figure 1. Chemical structure of Vitamin E (liquid at RT).

Methods: UHMWPE powder (GUR 1020 resin, MediTECH, Fort Wayne, IN) was mixed with AO at 0.075 w/w ratio to produce AO-Poly. Compression molded UHMWPE (GUR 1020, MediTECH Fort Wayne IN) was used as negative control group. GUR 1020 is a medical grade UHMWPE material with no additives. AO-Poly and GUR 1020 parts were gamma sterilized at 75 kGy and 115 kGy in vacuum packages (Steris Isomedix Services, IL). Physicochemical testing of AO-Poly and GUR 1020 samples were completed in aqueous and organic solvents (NAMSA test labs, OH). Non-volatile residue analysis of AO-Poly and GUR 1020 were conducted with HPLC after extraction with purified water (70 °C, 24 hrs), hexane (50 °C, 24 hrs), and isopropyl alcohol (70 °C, 24 hrs). Test extracts were further analyzed with LC/MS for identification purposes.

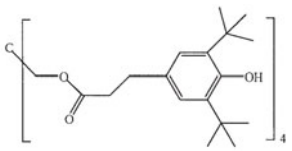

Figure 2. The chemical structure of **AO** (solid at RT).

Results: The migration stability of AO is a critical to protect the long term oxidative stability of crosslinked UHMWPE. Three different solvents were used to establish in-vivo diffusional stability of AO-Poly at 75 and 115 kGy gamma doses. Purified water was used to evaluate hydrophilic extractables, while hexane and isopropyl alcohol were used for lipophilic extractable in AO-Poly. 15-25 gr of AO-Poly and GUR 1020 were used for each extraction study. The eluate obtained from each solvent was clear and colorless. The HPLC studies of gamma irradiated AO-Poly detected less than 1 mg non-volatile residues regardless of the irradiation dose. The AO-Poly samples used in this study contained approximately 10-20 mg of **AO**. The non-volatile residual concentrations are the same when these results were compared to the negative control, GUR 1020 gamma irradiated at the same dose level. These results clearly indicated that elution of AO out of crosslinked AO-Poly (75, and 115 kGy) is not an issue. Further studies with eluates from each solvent were conducted with LC/MS in order to identify the residuals. The condition of LC/MS is given in Figure 3.

Parameter	Setting	
Column	Zorbax Eclipse XDB-C8 3.5 µm, 150 mm x 2.1 mm	
Flow Rate	0.3 mL/minute	
Injection Volume	2 µL	
Column Temperature	50°C	
Eluent A	HPLC Grade Water	
Eluent B	HPLC Grade Acetonitrile	
Time	Eluent A (%)	Eluent B (%)
0.00	50	50
10.00	0	100
30.00	50	50
Detector		
PDA Spectral Range	200-400nm	
Mass Spectrometer		
Ionization	ESI	
Detection	Quadrapole	
Spectral Range	50-1400 amu	

Figure 3. LC/MS parameters.

The standard solutions of Tinuvin P, BHT, and Irganox 1010 were prepared at 1, 5, and 10 ppm concentrations according to ASTM D5524-94 for determination of phenolic antioxidants in polyethylene. LC/MS profiles of AO-Poly and GUR 1020 eluates obtained from three different solvents used in this study were identical for both 75 and 115 kGy gamma doses. These results confirm the migration stability of AO in the crosslinked UHMWPE by showing that the presence of AO does not change the identity or amount of extractables.

Conclusions: Extraction studies conducted with AO-Poly and GUR 1020 in aqueous and organic solvents prove the migration stability of AO in 75 and 115 kGy irradiated UHMWPE.

Reference: 1) Kurtz SM. The Handbook of UHMWPE. New York, Academic Press, 2004.
2) Oral, E. Biomaterials, 27, 2434-2439.
3) Wolf, C. J of Mater Sci Mater Med, 17, 1323-31, 2006.