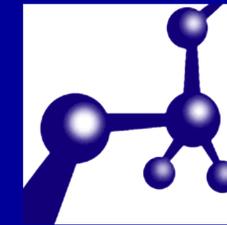


Sensitive Measurement of Vitamin E Concentration using OIT

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P 1177 Vitamin E (VE) is increasingly being used to improve oxidative stability of highly crosslinked ultra-high molecular weight polyethylene (UHMWPE), a prominent orthopaedic implant material. However, currently there is no sensitive technique for measuring VE concentration post-production. A method for sensitively determining low concentrations of VE as a function of position becomes crucial for confirming intended material properties including desired loading. Here we describe a novel method for quantifying VE concentration using oxidative-induction time (OIT) determined by differential scanning calorimetry. Current methods, such as Fourier-Transform infrared (FTIR) spectroscopy [1], are usually considered to be limited to levels of VE greater than 0.2 wt%, which is near the expected loading range for implanted UHMWPE (< 0.5 wt%), although some authors, using a more complex procedure, achieve determination down to 0.038 wt% [6]. OIT on the other hand is an ASTM method for measurement of oxidative stability and has a broad history of use with polyethylene, chiefly as an indicator of oxidative degradation and/or resistance [2-4]. We conducted OIT measurements on UHMWPE stabilized with varying concentrations of VE at three stages of processing. Comparison with initial VE wt% and processing conditions revealed a power-law relationship that could be used to determine the effective VE concentration of unknown samples, both as-mixed and post-processing, using an OIT master curve. The calibration curve therefore has potential utility in determining the effective concentration of any antioxidant (AO) in a sample pre-production or due to manufacturing processing (loss of effective VE due to consolidation or irradiation) or due to *in vivo* service.

Materials Methods

GUR 1050 powder (Ticona) was solvent blended with VE (DSM) in the following concentrations (by weight): 0.01, 0.02, 0.05, 0.10, 0.25, 0.28, and 0.38, verified gravimetrically using an Accelerated Solvent Extractor (ASE, Dionix, Inc.). Replicate measurements on one of the specimens (0.35 wt%) indicated that the uncertainty of the ASE measurement was approximately +/- 0.0012 wt%. Three sample sets were produced: un-processed powder, direct compression molded pucks, and direct compression molded pucks irradiated to 200 kGy (+/- 5%, 10 MeV electron beam). OIT analysis was performed on a Q1000 DSC (TA Instruments) according to ASTM D3895-98 [5]. Three specimens per sample from each set were tested. Powder samples were prepared by homogenization at 200 °C under nitrogen in the test pan for 10 minutes. Molded samples were prepared by using a 6 mm punch to cut discs from a microtomed 200 mm thick film. Analysis differed from that outlined in the standard. A method was developed equivalent to the Tangent method of the ASTM standard [5] that was insensitive to misleading or atypical features present in the oxidative exotherm. Vitamin E Index was also calculated as described elsewhere [7] using a BioRad FTS3000 Fourier-Transform infrared (FTIR) bench and UMA500 microscope and the average of ten positions adjacent to the OIT sample were reported. A comparison between the two techniques is shown in Figure 1.

Results & Discussion

The determined OIT values for the tested samples were compared to the nominal VE weight percent as shown in Figure 2. A power-law fit was applied using a non-linear algorithm (LabVIEW, National Instruments) of the form $VE = a \cdot OIT^b + c$. The unirradiated consolidated samples appear to follow a similar trend, although resulting in a slightly lower OIT. The irradiated samples indicated a significantly lower OIT. These data suggest that for the unprocessed materials, a simple power-law relationship exists between OIT and VE concentration dependent upon processing conditions. During processing, some of the VE (or whatever AO is present) will presumably be used to protect the UHMWPE, reducing the amount of VE available for further protection. OIT measurements should only reflect this reduced amount, termed here the effective VE concentration (EVC). For instance, since irradiation is known to generate many free-radicals, the EVC (and hence, OIT) of the irradiated samples is considerably lower than the original given concentration. Thus OIT may give insight into the amount of VE that is actually available to protect the UHMWPE *in vivo*, a figure that has never been available before. The results of the power-law fit can therefore be used to calculate the EVC for a specific processing condition. By plotting the ratio of the EVC to the VE, a measure of the reliability of the calculation can be determined (for the powder samples) as a measure of the impact of each of the processing conditions. These data are plotted in Figure 3. The powder samples are grouped tightly around a ratio of 1 (never more than 5.4% deviation), indicating that the power-law fit correctly predicts the unprocessed VE. The consolidated sample on the other hand exhibits systematically higher ratios than the powder (15-30% higher) consistent with some loss of Vitamin E activity due to exposure to high temperature and pressure. Finally, the irradiated samples exhibit a large VE/EVC ratio, consistent with a marked drop in effective stabilizer, a phenomenon expected after high radiation dose. The resulting calculations appear to hold for all samples with OIT values higher than 5 minutes regardless of processing conditions. OIT values of less than 5 minutes are believed to be near the resolution limit of the technique and these rapidly oxidizing samples do not behave in the same manner as the other samples. As a guide, the power-law fit predicts that an OIT of 5 minutes is equivalent to 0.0004% concentration.

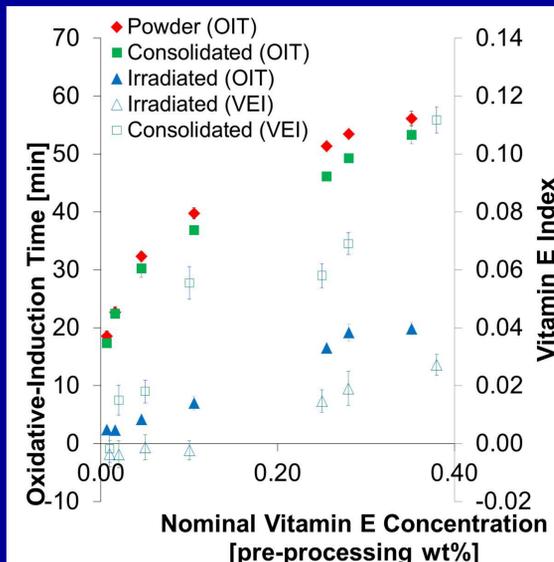


Figure 1: OIT and VEI v Nominal VE Conc. Error bars one standard deviation. Solid symbols are OIT, hollow symbols are VEI.

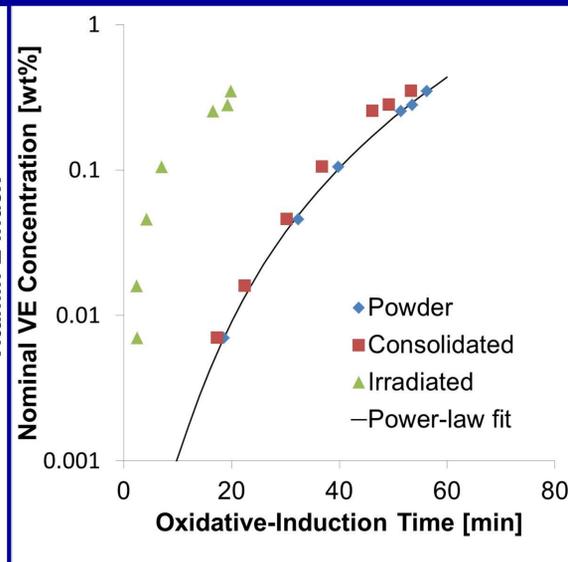


Figure 2: OIT value in minutes v Nominal Vitamin E conc after 3 different processing steps. Error bars one standard deviation.

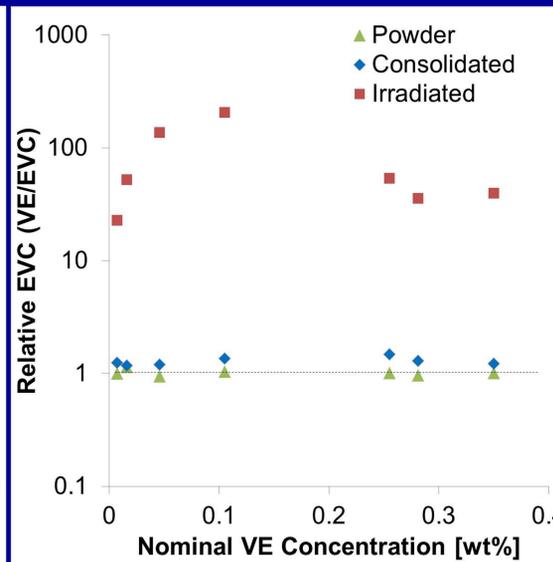


Figure 3: Relative EVC (the ratio of the Nominal VE concentration to the EVC) versus nominal VE conc.

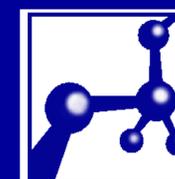
Conclusions

The OIT technique presented above provides a novel, sensitive method for determining the VE concentration in UHMWPE components. This method could be used for both QC and R&D purposes to evaluate effective VE levels after different processing conditions. The described master curve implies that, for given processing conditions, OIT can be used to determine the effective VE concentration of a blended and processed UHMWPE component. In addition, this technique is sensitive enough to detect changes in the effective VE concentration after simple compression molding of components, as well as more aggressive radiation processing, as indicated by the provisional detection limit of < 0.001 wt%. Thus, the technique could be used to investigate the influence of processing on effective VE concentration. We are currently extending this research with a round-robin study to validate intra- and inter-lab repeatability. Suggested future work includes determining the applicability of this method to other antioxidants.

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