JOURNAL OF THE MECHANICAL BEHAVIOR OF BIOMEDICAL MATERIALS 31 (2014) 21–30

Available online at www.sciencedirect.com

ScienceDirect

www.elsevier.com/locate/jmbbm

Research Paper

The antioxidant and non-antioxidant contributions of vitamin E in vitamin E blended ultra-high molecular weight polyethylene for total knee replacement

Alex Turner[a], *Yasushi Okubo*[a], *Satoshi Teramura*[a], *Yasuhito Niwa*[a], *Kento Ibaraki*[a], *Toru Kawasaki*[a], *Daisuke Hamada*[a], *Keita Uetsuki*[b], *Naohide Tomita*[a,]*

[a]*Department of Mechanical Engineering, Graduate School of Engineering, Kyoto University, Katsura Campus, Nishikyo-ku, Kyoto 615-8540, Japan*
[b]*R&D Center, Nakashima Medical Co. Ltd., 5322 Haga, Kita-ku Okayama 701-1221, Japan*

ARTICLE INFO

Article history:
Received 16 April 2012
Received in revised form
19 August 2012
Accepted 14 December 2012
Available online 29 December 2012

Keywords:
Vitamin E blended ultrahigh molecular weight polyethylene
UHMWPE
Total joint replacement
Tribological performance
Biological response
Delamination
Oxidation
Alpha-tocopherol

ABSTRACT

Vitamin E (VE) blended ultra-high molecular weight polyethylene (UHMWPE) has been developed in Japan as a material for use in total knee replacement (TKR). Various results have demonstrated that VE blended UHMWPE reduces the incidence of delamination failure and lowers the amount of wear produced during knee simulator testing. It was also found that wear particles from VE blended UHMWPE elicited a reduced biological response compared to conventional UHMWPE. A great deal of research concerning vitamin E (VE) stabilized ultrahigh molecular weight polyethylene (UHMWPE) has focused on VE's effects as an antioxidant and its ability to prevent the oxidative degradation of UHMWPE chains. However, other chemical and mechanical changes have been observed in VE blended UHMWPE that are unrelated to the oxidative protection that VE provides. This paper provides a general review of VE blended UHMWPE, with a particular focus on the non-antioxidant effects of VE. The potential application of VE blended UHMWPE in total hip replacement (THR), along with the differences in loading conditions between the knee and the hip are also discussed.

1. Introduction

Since its introduction in 1962, ultra-high molecular weight polyethylene (UHMWPE) has achieved outstanding success as a low-friction bearing material in total hip replacement (THR) (Charnley, 1995) and has been the cup material of choice for THR for most of the past half century (Kurtz, 2009). However, as both the concern for and understanding of osteolysis and aseptic loosening have grown (Abu-Amer et al., 2007; Bordini et al., 2007; Iannotti et al., 1986; Jasty, 1993; Kadoya et al., 1998), so too has the urgency for finding alternative bearing materials that can reduce the amount of wear debris produced over increasingly long implant lifetimes. In order to keep pace with these expanding and more stringent design requirements, a number of processing modifications have been developed to improve the wear resistance of UHMWPE.

**Corresponding author.* Tel./fax: +81 75 753 9201.
E-mail address: tomita.naohide.5c@kyoto-u.ac.jp (N. Tomita).

1751-6161/$ - see front matter © 2012 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.jmbbm.2012.12.006

One processing technique that has demonstrated success in total knee replacement (TKR), involves introducing *dl*-α-tocopherol (vitamin E) to the UHMWPE resin mixture prior to molding of the material. This VE blended UHMWPE was originally created to help to prevent delamination failure in TKR (Tomita et al., 1999). However, VE has been shown to be an excellent stabilizer of UHMWPE, helping to prevent the generation and proliferation of UHMWPE main chain free radicals. Vitamin E is an effective biological antioxidant, helping to prevent the oxidative degradation of cell membrane phospholipids. When added to UHMWPE, vitamin E (VE) performs a similar role, helping to prevent oxidation of the polyethylene chains (Wolf et al., 2006). As a result, when VE is added to UHMWPE, the material demonstrates a strong resistance to oxidation and experiences little to no mechanical degradation when subjected to accelerated aging (Kurtz et al., 2009; Shibata et al., 2003; Tanaka et al., 2008; Teramura et al., 2004).

Despite the original intention of Tomita et al. (Tomita et al., 1999), the oxidative protection that VE provides is generally considered to be the primary reason for incorporating VE into UHMWPE. However, due to the fact that VE is introduced into the UHMWPE resin mixture prior to material formation (as opposed to in VE doped UHMWPE, where VE is introduced after material formation), VE blended UHMWPE possesses a number of unique mechanical and chemical properties that are separate from the protection that VE provides against oxidative degradation. Among the more significant of these properties, VE blended UHMWPE has demonstrated an increased resistance to wear in both pin-on-plate testing and knee simulator testing compared to unaged conventional UHMWPE (Oral et al., 2009; Teramura et al., 2008). Recent results have also demonstrated that wear particles from VE blended UHMWPE elicit a reduced biological response from macrophages cultured in vitro (Teramura et al., 2011).

In this paper, a brief review of VE blended UHMWPE will be presented, including a general description of the oxidation process that occurs in UHMWPE and the manner in which VE helps to suppress that oxidation. However, the primary focus of the paper will be on the non-antioxidant roles of VE within UHMWPE; experiments exploring these chemical and mechanical roles and the related tribological behavior will form a majority of the text. Special discussion will also be given to the application of VE blended UHMWPE in total hip replacement (THR).

2. Search strategy and criteria

Parallel searches were performed using the PubMed, Web of Science, and Scopus SciVerse databases using the keywords: "vitamin E" and "polyethylene." This resulted in 136 (PubMed), 302 (Web of Science), and 388 (Scopus SciVerse) positive matches, which were then individually screened for articles dealing specifically with orthopedic UHMWPE materials produced via blending with vitamin E prior to solidification, i.e. VE blended UHMWPE. However, a number of articles that were relevant to some of the specific issues discussed in this paper, such as artificial joints and osteolysis, were also included. In total, 53 articles, two theses, and one book were reviewed for this report.

3. Vitamin E and oxidation in UHMWPE

As mentioned in the Introduction, vitamin E's primary function in the body is to protect cell membrane phospholipids from oxidative damage. The oxidation of the hydrocarbon chains on these phospholipids is similar to the oxidation of the polyethylene chains in UHMWPE (Costa and Bracco, 2009). In each case, the presence of radicals along a hydrocarbon chain and a supply of available oxygen are all that is needed for oxidation to begin. In UHMWPE, main chain radicals can be generated during gamma sterilization, when the material is exposed to high energy gamma rays, cleaving both C–C and C–H bonds (Ormerod, 1965). However, lower energy radiation, such as exposure to UV rays, can also lead to the generation of main chain radicals in UHMWPE (Giesse and De Paoli, 1988). Once formed, these radicals can combine with available oxygen to cause an oxidation cascade that eventually leads to chain scission and a degradation of the material's mechanical properties. Although a slight simplification, the oxidation cycle that occurs in UHMWPE is similar to Bolland's Cycle (Costa and Bracco, 2009), which describes oxidation in short chain hydrocarbons, outlined in Fig. 1. In the presence of oxygen, an alkyl radical is transformed into a peroxy radical (Fig. 1A). This peroxy radical is then able to cleave a hydrogen from a neighboring chain, resulting in a hydroperoxide and a new alkyl radical (Fig. 1B). With this new alkyl radical and more oxygen, the entire process is able to repeat (Fig. 1C), leading to further radical generation. Other products, such as carboxylic acids, alkoxy radicals, ketones, and esters, are also formed (Al-Malaika, 2004). Ultimately, scission of the polyethylene chains can occur, causing deterioration of the mechanical properties of the material.

Vitamin E, or rather alpha tocopherol, when added to UHMWPE has been shown to suppress this oxidation cycle (Bracco et al., 2007; Jahan and Walters, 2011; Wolf et al., 2006). Alpha tocopherol is the most preferentially absorbed and most biologically active member of the vitamin E family (Muller et al., 2010), which consists of eight separate antioxidant compounds: four tocopherols and four tocotrienols, with α, β, γ, and δ versions of each. The specific alpha tocopherol form normally used in VE blended UHMWPE is *dl*-α-tocopherol (shown in Fig. 2), which is a synthetic version of the molecule and is composed of a mixture of all eight stereoisomers (Al-Malaika, 2004). For the purposes of this paper, *dl*-α-tocopherol will be referred to as vitamin E (VE) and all references to VE will refer to this molecule.

VE's strength as an antioxidant is derived from its ability to donate a hydrogen atom to an oxidized molecule without furthering or renewing the oxidation of surrounding molecules. VE's phenolic hydrogen, located on the molecule's chroman ring, is easily extractable and can be used to reduce a sufficiently close free radical. The VE radical that is generated following donation of the phenolic hydrogen is molecularly stable, preventing the generation of any new free radicals. In UHMWPE, VE is able to suppress the oxidation cascade by reducing both alkyl and peroxy radicals (Bracco et al., 2007). However, due to the relative immobility of both peroxy radicals and VE itself, stabilization following material formation occurs primarily through the reduction of the more