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Chemical Characterization of Ultra High Molecular Weight Polyethylene Based Tibial Inserts After Ethylene Oxide Sterilization

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Abstract

Ultra-high molecular weight polyethylene (UHMWPE) has become the gold standard for total joint replacements such as tibial inserts because of its chemical inertness, superior mechanical properties, and biocompatibility. Ethylene oxide sterilization is one of the most common and effective methods used, especially for the sterilization of polyethylene-based polymeric implants. However, variable sterilization conditions can cause a change in the chemical structure of the polymeric material, which affects its mechanical properties and lifetime. The aim of this study is to investigate whether the chemical structure of UHMWPE tibial inserts sterilized with ethylene oxide undergoing certain conditions remains the same. Chemical characterization studies were performed with Fourier transform infrared spectroscopy, Raman spectroscopy, X-ray diffractometer, differential scanning calorimetry, thermogravimetric analysis, mass spectrometry and elemental analysis techniques recommended for polymeric materials in ISO 10993-8:2020 standard. According to the FTIR results, the spectra of the non-sterile and sterile tibial inserts were compared, and it was determined that the similarity between them was 99.97%. XRD results revealed that after ethylene oxide sterilization, there was no significant shift in the Bragg (1 0 0) peak. The percentages of crystallinity calculated from the fusion enthalpies determined by DSC of sterile and non-sterile samples are 54.3% and 53.3%, respectively. Characterization results revealed that there was no significant change in molecular structure, crystallinity, elemental composition of UHMWPE materials after ethylene oxide sterilization. These results can provide assurance that tibial inserts keep their physical, chemical, and mechanical properties after sterilization.

1. Introduction

Every year, millions of patients are implanted with medical devices to improve their quality of life and/or replace all or part of the biological structure or act as a part of it. Implantable medical devices continue to be one of the important research and development areas due to their potential applications in healthcare. Nowadays, bioimplants are being used in different parts of the body for diverse applications such as orthopedics (hips or knees), dentary, cardiovascular stents, neural prosthetics, pacemakers, defibrillators and drug delivery systems [1]. Implantable devices are biocompatible materials covering various material classes such as metallic, ceramic, and polymeric materials [2-4].

Polymeric biomaterials are used as a substitute or adjunct to metal alloys in trauma and orthopedic implant devices due to their mechanical, chemical, thermal and biostable properties as well as their biocompatible nature [4].

For this reason, many absorbable and non-absorbable polymeric implants approved by the Food and Drug Administration (FDA) have been used in clinical practice for decades [5]. Polyglycolic acid, polylactic acid, polydioxanone, polyvinyl alcohol, polyglycolide-L-lactide, polyethylene oxide, polyethylene glycol and polycaprolactone are the most widely used absorbable synthetic polymers [6, 7]. This type of polymer is used in various fields of orthopedics and trauma surgery, especially as absorbable sutures, and screw pins [6]. Polyethylene terephthalate, polypropylene, poly(ether–ether–ketone), polyamide, polyvinyl chloride, polystyrene, polycarbonate,

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polyurethane, acrylonitrile butadiene styrene and polyethylene are non-absorbable polymers used in the manufacture of many medical devices such as surgical sutures, vascular grafts, spinal cages, stents, hernia mesh, artificial knee and hip joints [8-12].

Polymer biomaterials are chosen for biomedical applications based on various criteria including molecular weight, chemical structure, surface and mechanical properties, while their properties such as thermal (melting point, glass-transition temperature, etc.), solubility and degradation behaviors are primary considerations affecting the selection of scaffold production technique [13].

Synthetic polymers such as polylactic acid, polycaprolactone, poly(ether–ether–ketone) and polyethylene have become highly suitable biomaterials to meet bone tissue requirements due to their biocompatibility, robust mechanical properties and adaptability [14]. Among these polymers, polyethylene is a favorite material due to its low price, easy fabrication and forming process, availability, versatility, and widespread clinical success.

Polyethylene materials are light, flexible, biologically stable, chemically inert and resistant to many organic solvents at room temperature [15]. Because of its variable molecular weight, density and chain structure (branching), it has been categorized into five different types by the American Society for Testing and Materials (ASTM), each with different thermal, mechanical, chemical, electrical and optical properties: low-density polyethylene, linear low-density polyethylene, medium density polyethylene, cross-linked polyethylene, high-density polyethylene and ultra-high molecular weight polyethylene (UHMWPE) [16].

UHMWPE is an FDA-approved polymer that has been used as a medical device for decades. UHMWPE is widely used in orthopedic implants due to its excellent biocompatibility, extremely resistance to abrasion and corrosive chemicals, low wear volume, high tensile strength, low friction coefficient and high crystallinity [17, 18]. UHMWPE was first used in 1962 as joint replacement in total hip arthroplasty combined with a metal femoral head [16]. Today, it is widely used in hips, knees, shoulders, ankles, elbows, wrist joints as well as spinal discs [19]. All these joint replacements comprise at least two fragments articulating with one another. For example, a knee replacement has a metal femoral part, shaped to simulate the articular surface of a femur, and a tibial insert comprising mainly of UHMWPE with a metal backing socket (Figure 1) [20]. In this type of prosthesis, UHMWPE has a critical task, which is usually placed between metal components, both facilitating the movement of metals and preventing the direct transfer of load from metal to metal [7].

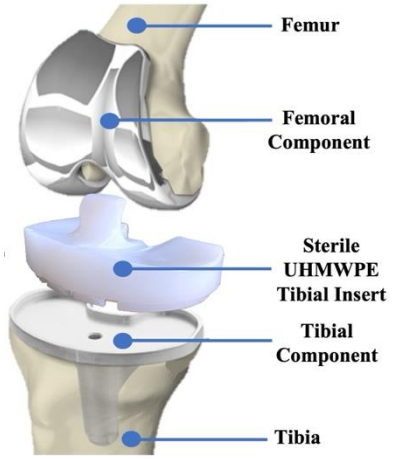

Figure 1. The components of a total knee replacement.

Medical devices can be classified as critical, semi-critical and non-critical according to the degree of infection risk in their use. Implants such as tibial inserts placed on the sterile part of the patient's body are critical devices with a high risk of infection [21]. Therefore, it is extremely important to sterilize the implant in a way that destroys all infecting microorganisms such as bacteria, viruses, fungi, yeasts and molds before the surgical operation [22]. There are many techniques used for sterilizing medical devices. Sterilization with autoclaving, dry heat, ozone gas, hydrogen peroxide vapor, low-temperature gas plasma, glutaraldehyde solution, peracetic acid, formaldehyde, microwave, gamma rays, ultraviolet light and ethylene oxide are some of them [21, 23]. Among these techniques, the most widely used sterilization technique for polymeric materials is ethylene oxide.

Ethylene oxide is an exceptional agent that is frequently used in the sterilization of medical devices due to its effective bactericidal, sporicidal and virucidal activity [24]. The antimicrobial effect of ethylene oxide is because of its inhibition of normal cellular metabolism and replication by causing cell wall, protein, DNA and RNA damage in the microorganism through chemical interactions [25]. The effectiveness of sterilization depends on the ethylene oxide concentration, temperature, humidity, exposure time to the gas and packaging material [26]. Moreover, these conditions can change the physico-chemical and mechanical properties of the polymeric implant, which negatively affects its performance in the body [27, 28]. For example, it has been reported that the strength of the polymer decreases according to the decrease in the molecular weight of the polymer under unsuitable sterilization conditions [29]. Changing the molecular weight impairs the mobility of the polymer chains, which causes the life, absorption, and mechanical properties of the polymer to change [25, 30]. Also, it has been reported in the literature that after sterilization, changes in the molecular properties

of bioabsorbable polymers considerably influence the biodegradation kinetics and the performance time [31, 32]. Hence, it is highly vital to detect the suitable sterilization methods and conditions for polymeric implants with various physical, chemical, and biological analyses. Medical device certification bodies also require medical device manufacturers to chemically compare the raw form of an FDA-approved material with the final product that has undergone shaping and sterilization processes.

In this study, comparative chemical characterization of the non-sterile and sterile versions of the tibial insert made of UHMWPE material was performed according to ISO 10993-18 (Biological evaluation of medical devices-Part 18: Chemical characterization of medical device materials within a risk management process). The aim of this study is to clarify whether there is a change in the chemical structure of medical devices produced from UHMWPE after being sterilized with ethylene oxide under the same conditions.

2. Materials and Methods

2.1 Materials

A commercial product, Total knee prosthesis tibial inserts (P/S, 70/15 mm, Hyperflex, UHMWPE) was obtained from a local medical device company (Ankara, Turkey).

2.2. Ethylene oxide sterilization procedure

The ethylene oxide sterilization process was carried out in a sterilization center according to ISO 11135 requirements. Briefly, the UHMWPE tibial inserts were preconditioned for 4 h at 50 ± 5 °C in 70–90% of relative humidity in a separate chamber. And then, the samples were in the ethylene oxide sterilization chamber. Throughout the sterilization (18 cycles), inside the sterilization chamber, preconditioning was through for 80 min at 50 ± 5 °C. Thenceforth, the samples were exposed to a gas mixture of 20% ethylene oxide and 80% carbon dioxide for 8 h. After sterilization, drying was done at 40 °C under a vacuum (1 torr) for 50 min (vacuum: 40 mins and nitrogen charging: 10 mins). Non-sterile and sterile UHMWPE tibial inserts are shown in Figure 2.

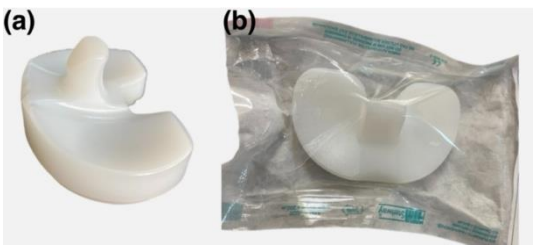

Figure 2. Non-sterile (a) and ethylene oxide sterilized (b) UHMWPE tibial inserts.

2.3. Chemical Characterization

2.3.1. Fourier transform infrared spectroscopy

Functional group analysis of the non-sterile and sterile tibial inserts was performed according to ASTM E1252 by FTIR spectroscopy (Bruker Vertex 70 V, USA). The percentage of similarity between the FTIR spectra of the materials was determined by the FTIR/OPUS software (4.2 Version, Copyright© Bruker Optics GmHb, USA).

2.3.2. Raman spectroscopy

Another functional group analysis was performed using a Bruker Senterra Raman instrument (laser wavelength: 532 nm, laser energy: 20 mW, duration: 60 sec, frequency: 50-4500 cm^{-1}).

2.3.3. X-ray diffraction

The phases structure of the sterile and non-sterile samples was analyzed using a X-ray diffraction (XRD, Empyrean, Malvern Panalytical) with 40 kV CuKα radiation (λ = 1.54056 Å). Samples were analyzed under the same scanning conditions (2θ = 10–80°, step size = 0.013°, scan rate = 2.0° min^{-1}). The d-spacing values of the samples were determined by Profex XRD software (Version 4.3.6), and the crystallite size values were determined by the Scherrer Equation [33].

2.3.4. Differential scanning calorimetry

Thermal properties of polymeric tibial inserts were analyzed by differential scanning calorimeter (DSC, Q 2000, TA Instruments, USA) with a heating rate of 10 °C min^{-1}, in a nitrogen gas atmosphere up to 400 °C, using an aluminum T-*zero* hermetic pan. Also, with DSC, the overall crystallinity (X_c, %) of polymers was calculated by the following equation:

$$X_c\ (\%) = \frac{\Delta H_f}{\Delta H_{100}}\ x\ 100 \qquad (1)$$

where ΔH_f is the heat of fusion and ΔH_{100} is the melting enthalpy of the 100% crystalline polymer.

2.3.5. Thermogravimetric analysis

The thermal degradation steps of the materials were analyzed with a thermogravimetric analyzer (TGA, Q 500, TA Instruments, USA) under certain conditions (nitrogen gas atmosphere, 10 °C min^{-1} heating rate, ceramic pan).

2.3.6. Mass spectrometer analysis

Mass spectrometer (MS) analyses of tibial inserts were performed on a Shimadzu QP 2010 GC–MS system using DI (direct injection) method over MS. The MS scan parameters included a mass scan range of 20–1090 m z^{-1}, an event time of 0.5 s, and a scan speed of 2500 µm s^{-1}. The ion source temperature was set to 350 °C with a heating rate of 10 °C min^{-1}.

2.3.7. Elemental analysis

Carbon(C), nitrogen (N), hydrogen (H) and sulfur (S) contents of the materials were determined with a CHNS elemental analyzer (vario MICRO cube, Elementar, Germany).

3. Results and Discussion

3.1. Functional group analysis

Depending on the ambient conditions (such as temperature, humidity, and exposure time) during the sterilization process, a chemical reaction may occur between the ethylene oxide gas and the polymeric material. This causes the physical and mechanical properties of the polymeric material to change. FTIR provides important information to determine the chemical bond changes of polymeric materials. Therefore, whether or not the chemical bond structure of the UHMWPE tibial inserts changed after sterilization was analyzed by FTIR (Figure 3). Since UHMWPE is a polyolefin type, the sharp absorption peaks at 2915 cm^{-1} and 2848 cm^{-1} are characteristic asymmetric and symmetric stretching vibration bands of CH_2 groups, respectively [15, 33]. Other clear peaks occurring at 1471 cm^{-1} and 722 cm^{-1} can be attributed to C-H vibration deformation and C-C rocking vibrations in the CH_2-CH_2 groups, respectively [34]. Meanwhile, UHMWPE sterilized with ethylene oxide is likely to be oxidized. Oxidation can be determined by looking at changes in 1720 cm^{-1} (carbonyl groups) [35, 36]. The absence of any absorption band at 1720 cm^{-1} is strong evidence that the material is not oxidized after ethylene oxide sterilization (Figure 3b). The spectra of non-sterile and sterile tibial inserts were compared and the similarity between them was found to be 99.97%. According to the results of the FTIR, there was no change in the chemical bond structure of UHMWPE, which was sterilized with ethylene oxide under certain conditions.

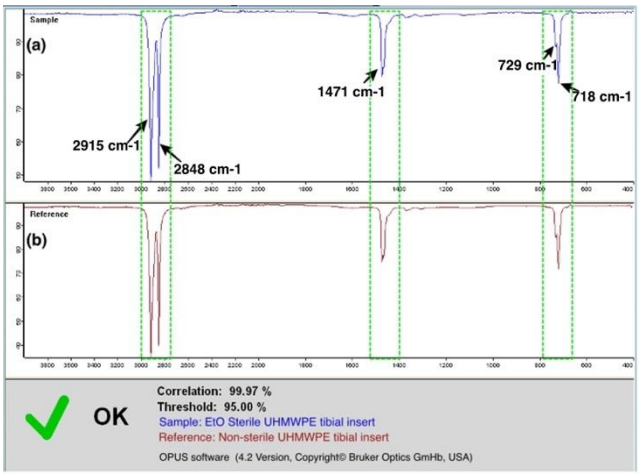

Figure 3. Comparison of the FTIR spectra of UHMWPE tibial inserts: (a) sterile, (b)non-sterile (scan speed: 32 cm^{-1}, resolution: 4 cm^{-1}).

3.2. Molecular structure analysis

Raman spectroscopy sensitively analyzes changes in the molecular structure level of polyethylene, such as the degree of crystallinity, which is a key factor in determining polyethylene density [37]. The change in the molecular structure and crystallinity of UHMWPE tibial inserts after sterilization was investigated by Raman (Figure 4). The peaks occurring in the region between 1150 cm^{-1} and 1500 cm^{-1} are attributed to the CH_2 groups in the crystalline and amorphous phases, respectively. The peaks between 1000 cm^{-1} and 1150 cm^{-1} are attributed to the symmetric and asymmetric C–C stretching vibrations [38, 39]. In addition, the sharp peaks seen at 2825 cm^{-1} and 2970 cm^{-1} belong to the stretching vibrations of the CH_2 groups [37]. When the Raman spectra of sterile and non-sterile tibial inserts are compared, it is seen that they are in harmony and there is no detectable difference.

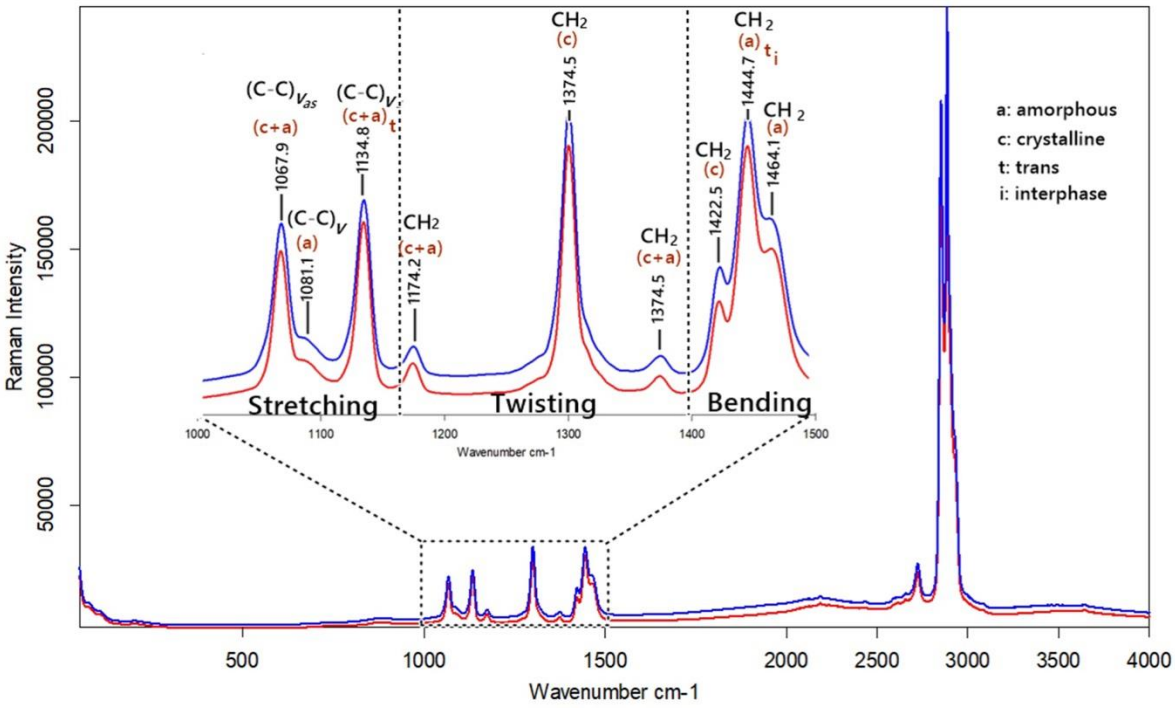

Figure 4. Raman spectra of sterile (blue) and non-sterile (red) UHMWPE tibial inserts.

3.3. Crystallinity and phase analysis

UHMWPE is a linear homopolymer whose chain curves show the local order in the form of crystalline lamella among amorphous matrixes [35]. Sterilization methods such as gamma-ray, ion beam, ultraviolet and ethylene oxide may change the crystallinity of the polymer by causing oxidative degradation, depending on the sterilization conditions [15, 35, 40]. It has been reported that the degree of crystallinity affects the mechanical properties of polymers such as Young's modulus, strength, fatigue, yield stress and shrinkage [41-43]. XRD was used to observe the variation in phase structure or crystallinity of sterile and non-sterile materials, and the diffractograms are shown in Figure 5. The peaks at angles 2θ of 21.49°, 23.91° and 29.71° match the (1 1 0), (2 0 0) and (0 2 0) orthorhombic lattice planes of the semi-crystalline UHMWPE, respectively [33, 43, 44]. The 2θ, d-spacing and crystallite size values corresponding to the (1 1 0) and (2 0 0) planes of sterile and non-sterile materials were shown in Table 1. The d-spacing and crystallite size values of UHMWPE tibial inserts are almost the same after sterilization. In addition, there was no remarkable shift in the Bragg (110) peak, which demonstrates that there is no change in the inter-planar spacing [35].

Table 1. 2θ, d-spacing and crystallite size values of non-sterile and sterile UHMWPE tibial inserts.

Sample	2θ [°]	d-spacing [A°]	Crystallite Size [nm]
Non-sterile	21.49	4.133	36.70
	23.91	3.716	33.91
Sterile	21.42	4.144	37.70
	23.87	3.725	33.90

3.4. Comparison of thermal properties

Besides the thermal properties of polymers such as glass transition (Tg) temperature, melting temperature (Tm), oxidation temperature and crystallization temperature (Tc), DSC was used to analyze whether decomposition is endothermic or exothermic. Moreover, the crystallinity degree (%) of thermoplastic polymers can be calculated by the enthalpy (heat) of fusion related to the melting transition of the polymer. Crystallinity is ascertained by normalizing the observed heat of fusion to that of a 100% crystalline sample of the same polymer. In the DSC thermograms shown in Figure 6, the melting temperatures of sterile and nonsterile UHMWPE tibial inserts were determined as 142.05 °C and 142.30 °C, and the heats of fusion were 159.1 J g^{-1} and 156.3 J g^{-1}, respectively.

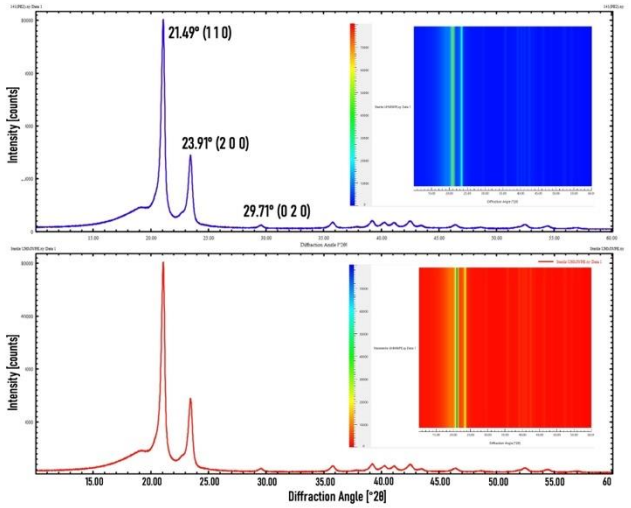

Figure 5. X-ray diffraction patterns of the sterile (blue) and non-sterile (red) UHMWPE tibial inserts.

The enthalpy of fusion for 100% crystalline polyethylene is 293 J g^{-1} [43, 45]. The percentages of crystallinity of sterile and nonsterile samples were calculated as 54.3% and 53.3%, respectively. There was no considerable change in the melting point and crystalline degree of the UHMWPE tibial insert after the ethylene oxide sterilization. Therefore, it can be said that the ethylene oxide sterilization temperature (50 °C) and the exposure time (8 h) at this temperature do not cause any chemical and physical changes in the chain structure of UHMWPE. We could not find a comparison study after ethylene oxide sterilization in the literature; however, there are studies examining the effect of gamma-ray sterilization conditions on the melting temperatures and crystalline degrees of UHMWPE with DSC [46, 47].

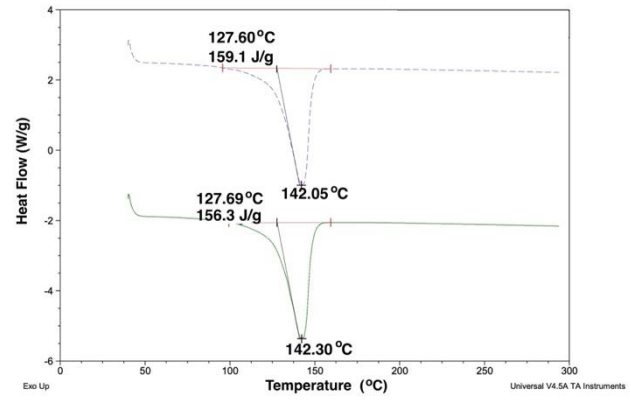

Figure 6. DSC thermograms of sterile (green) and nonsterile (blue) UHMWPE tibial inserts.

3.5. Comparison of thermal stabilities

During the ethylene oxide sterilization process, the polymeric material is exposed to temperature, humidity, pressure, and chemical gas. For this reason, some physical and chemical changes may occur in the structure of the polymer, which also affects its thermal stability. TGA is a thermal analysis method that determines mass changes as a function of time and temperature [43, 44]. The thermal stability of sterile and non-sterile UHMWPE tibial inserts was investigated by TGA (Figure 7). Nonsterile UHMWPE is thermally stable up to 450 °C and exhibited a single-step decomposition at subsequent temperatures with a maximum decomposition temperature of 523.6 °C. The results agree with the literature [43, 48, 49]. After ethylene oxide sterilization, no mass loss of any evaporating or volatile components was observed up to 450 °C. In addition, there is no significant change in the maximum decomposition temperature (524.16 °C). The residual masses of sterile and non-sterile tibial inserts at the end of 600 °C were determined as 0.35% and 0.36%, respectively. As a result, no physical and chemical changes were detected, that would affect the thermal stability of the materials after the sterilization process.

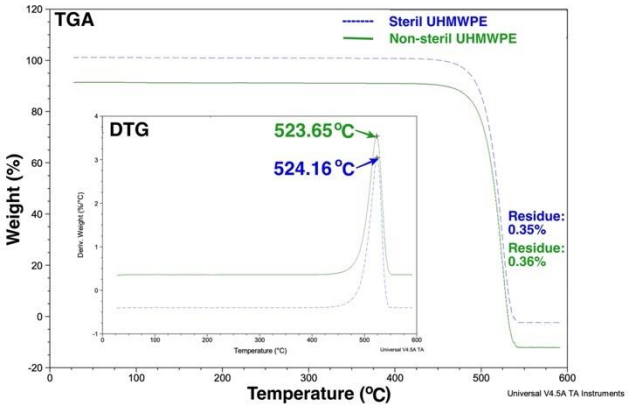

Figure 7. TGA and D-TGA curves of sterile and nonsterile UHMWPE tibial inserts.

3.6. Mass spectrometer results

MS is an important technique used to identify and characterize the degradation products of polymeric materials [50]. MS was also used to determine if the chemical structure of the UHMWPE tibial inserts changed after the ethylene oxide sterilization. Polyethylene is a very high molecular weight hydrocarbon, and its degradation products are normal hydrocarbons such as oligomers. Among these hydrocarbons, there may be alkadienes, alkenes and alkane groups such as long-chain dodecadiene, dodecene and dodecane [51]. With the change of the

molecular structure of the polymer after the sterilization process, the ionized decomposition products also partially change. The mass spectrum of the degradation products was compared according to the mass/charge (m/z) ratio of polyethylene, and it was determined that the degradation products of the tibial inserts were almost the same (Figure 8). Therefore, this high similarity can be attributed to both the preservation of the chemical structure and the absence of ethylene oxide residue after sterilization. Meanwhile, the ethylene oxide residue is analyzed according to the methods and conditions specified in ISO 10993-7 (Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals) [25, 52].

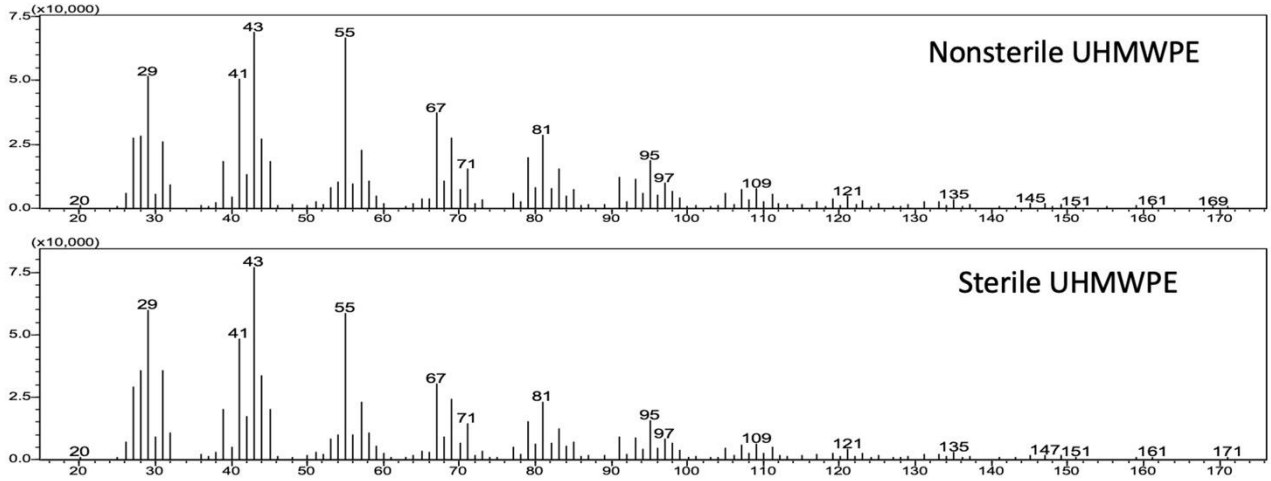

Figure 8. Mass spectra of sterile and nonsterile UHMWPE tibial inserts.

3.7. CHNS elemental analyses results

Elemental analysis is an extensively used technique to measure the amount of carbon (C), hydrogen (H), nitrogen (N), sulfur (S), and oxygen (O) in the structure of many materials [53]. The theoretical C and H content of polyethylene, whose repeating unit has the chemical formula $–(C_2H_4)_n–$ (n: degree of polymerization) is 85.63% and 14.26%, respectively [54]. During the ethylene oxide sterilization, the carbon, hydrogen, nitrogen, sulfur, and oxygen contents of the polymeric material may change when exposed to temperature, ethylene oxide, carbon dioxide, nitrogen gases, humidity (H_2O) and air. Therefore, C, H, N and S contents of sterile and nonsterile tibial inserts were determined by CHNS/O elemental analysis (Table 2). The average carbon and hydrogen content of the nonsterile material were determined as 85.61% ± 0.3% and 13.95% ± 0.007%, respectively. The carbon and hydrogen contents of the sterile tibial insert were determined as 85.61% ± 0.3% and 14.062% ± 0.064%, respectively. Although there does not seem to be a significant difference in the carbon and hydrogen contents after sterilization, these minor changes may be due to a residue. The residue may be caused by ethylene oxide or other contaminants, but it is very important to analyze ethylene oxide residue after sterilization, especially since ethylene oxide gas is very toxic and carcinogenic [25].

Table 2. Carbon, Hydrogen, Nitrogen and Sulfur contents of non-sterile and sterile UHMWPE tibial inserts.

Sample	C [%]	H [%]	N [%]	S [%]
Non-sterile	85.58	13.978	0.00	0.00
Non-sterile	85.63	13.991	0.00	0.00
Non-sterile	85.63	13.986	0.00	0.00
Mean Value	*85.61*	*13.985*	*0.00*	*0.00*
Deviation	*0.03*	*0.007*	*0.00*	*0.00*
Sterile	85.71	13.989	0.00	0.00
Sterile	85.65	14.101	0.00	0.00
Sterile	85.67	14.097	0.00	0.00
Mean Value	*85.68*	*14.062*	*0.00*	*0.00*
Deviation	*0.03*	*0.064*	*0.00*	*0.00*

4. Conclusions

In the last decade, there has been a tremendous increase in the number of implantable medical devices based on UHMWPE, especially as part of joint prostheses. There is no single standard method recommended by the FDA for the sterilization of polymeric implants. Manufacturers must optimize the sterilization conditions according to the type of polymer used, molecular weight (such as LDPE, HDPE, UHMWPE), and shape and size of the device. Ethylene oxide is one of the most widely used and safe methods for the sterilization of UHMWPE

materials. However, depending on the sterilization conditions, the physical, chemical, and mechanical properties of the polymer material may be affected, which is of vital importance, especially for polymeric implants used in knee prostheses. In the present study, it was investigated by various instrumental techniques if there was a change in the chemical structure of UHMWPE tibial inserts after sterilization. The agreement between the FT-IR spectra of the non-sterile and sterile samples was 99.97%. The high agreement between both FT-IR and RAMAN spectra revealed that there was no significant change in the chemical bond structure of the materials after sterilization. The percentages of crystallinity of sterile and non-sterile samples were calculated by DSC as 54.3% and 53.3%, respectively. The agreement between the XRD results also supports the DSC results. These results support that the polymer chains have not undergone a change that would affect the mechanical properties of the material. Therefore, in this study, it has been proven that there is no significant change in the chemical structure of tibial inserts after ethylene oxide sterilization.

Ethylene oxide is thus a viable method for sterilization of UHMWPE tibial inserts. However, the chemical structure and mechanical integrity of UHMWPE materials may deteriorate when exposed to very high doses.

Declaration of Ethical Standards

The author of this article declares that the materials and methods used in this study do not require ethical committee permission and/or legal-special permission.

Conflict of Interest

The author declares that he has no competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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