Study of the interaction of ionizing radiation in polyurethane polymer films as biomaterial

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Abstract: New materials are being studied and widely applied in the health area, highlighting biocompatible polymers as the most versatile. Among these polymers, we developed the methodology for the manufacture of Thermoplastic Polyurethane films for application as Biomaterials. The proposed sterilization by ionizing radiation requires the study and characterization of the material to evaluate possible losses or modifications, due to the influence that the radiation can cause in the polymer chains, losing the characteristics for the purpose used. Therefore, the present work evaluates, through chemical and physical–chemical characterization, the possible extension of the changes caused by the radiation in the polyurethane film. The material is produced in an environment with controlled temperature and humidity and subjected to increasing doses of gamma (15, 25 and 50 kGy), ethylene oxide and plasma as comparative techniques. The techniques DSC (Differential Scanning Calorimetry), TGA (Thermogravimetry), FTIR-ATR (Fourier Transform Infrared Spectrometry), SEM (Scanning electron microscopy) and OCT (Optical coherence tomography), have proved that the material, after applied the sterilization techniques, maintains its physical–chemical characteristics and does not suffer any modifications after the treatment.

Keywords: Thermoplastic Polyurethane. Biomaterial. Gamma Radiation. Characterization. Polymer.

Introduction

It is extremely difficult to find materials that have biocompatibility properties, since human organism is a great challenge due to its extreme complexity. The science of biomaterials is an important part of the nearly 300,000 products used in the health area. In the year 2000, the world market for biomaterials was estimated at US$ 23 billion, with a growth rate of more than 12% per year, reaching US$ 40 billion in 20051. There has been a significant expansion in the global biomaterials market in recent years.

US$ 25.6 billion worldwide, with the following distribution: 43% in the USA, 33% in Europe, 3% in Asia and the Pacific, 2% in Brazil and 19% in the rest of the world2. In 2012, this market reached US$ 44 billion and, in 2017, a total of US$ 88.4 billion, with a growth rate of 22.1% per year, the expectation of expenditures in 2019 exceeds US$ 33 billion with implantable biomaterials. Supposedly, this market will continue to be led by North America, Europe and Asia over the next few years3.

The accelerated growth observed in the biomaterials market can be attributed to three main reasons: the aging of the world population, with the increase in life expectancy; increasing purchasing power and life standard in developing countries, which facilitate access to treatments of various types of disease; and technological improvements in addressing previously untreatable diseases4.

Biomaterials are defined as: “any substance or combination thereof, synthetic or natural, which may be used for a time, together or as part of the system which it treats, or restores a tissue, organ or function in the organism”5. Biomaterials must produce biological or systemic responses and must not present toxicity, carcinogenic substances, antigenic and mutagenic agents. Due to different applications, the devices may have long-term applications, such as permanent prosthetics, cardiac valves and lining6.

In 1959, the first report of the use of polyurethane in biomedical applications was published, being explored as cardiac valves in an artificial heart. In this work the team introduced the valves in 51 dogs, evaluating the biocompatibility of the material followed by their complications7.

It is important to highlight, experimental studies of an expandable stent valve, with polyurethane leaflets, implanted by catheter, with the longest follow–up (21 months), have demonstrated the integrity of the ultra-structure of this material, replacing the pulmonary valve8.

The development of new polymeric materials, especially in the medical field, the polyurethane among them, had as one of its main advantages the adaptation of the mechanical properties and degradation kinetics to meet various applications, having the capacity of being manufactured with various techniques and morphological characteristics9.

Polyurethanes are formed from the reaction of diisocyanates and polyoléfins as viewed in Fig.1, having several combinations and generating a large number of different polyurethanes.

The polyurethane chain consists of an alternating sequence of flexible and rigid segments. The polyol grants

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the elastomeric characteristics to the polymer, being characterized by the flexible segments of the material, whereas the diisocyanate will match the characteristics of the rigid segment of the material, such as hardness, toughness and strength\textsuperscript{10}.

Polyurethane has a wide variety of densities and hardness, which change according to the type of monomer used and according to the addition or not of modifying properties. The cure rate is influenced by the reactivity of the functional group, and its functionality by the number of isocyanate groups. The mechanical properties are influenced by the tertiary structure of the molecule. The choice of the diisocyanate also affects the stability of the polyurethane when exposed to light. The polyurethanes synthesized with aromatic diisocyanates become yellowish when exposed to ultraviolet light, whereas those synthesized with aliphatic diisocyanates are stable\textsuperscript{11} (Figura 1).

When developing a new product, it is also necessary to develop a methodology for the sterilization of the material. Currently, the most applied methodology for sterilization of medical products is with Ethylene Oxide, which can leave toxic residues causing possible complications in the patient. Sterilizers that operate at low temperature using hydrogen peroxide as the substrate for plasma formation are also widely used for heat sensitive materials, but for large quantities it is limited.

Among the methods developed for sterilization, ionizing radiation can be used in the health area for its effectiveness in eliminating contaminants from several sources\textsuperscript{12}. The use of ionizing radiation allows the sterilization of these materials at low temperatures, having as a main advantage the minimum handling of the material, which can be irradiated after its final packaging, due to its excellent penetrability, allowing full access to the material.

The ionizing radiation has two mechanisms of action, one being of direct effect on the molecules of the microorganisms, breaking, injuring and fusing the structures; the other effect is the indirect one that is caused by the formation of free radicals with the water radiolysis, in which they interact with the molecules in a chain reaction culminating in the death of microorganisms\textsuperscript{13}.

Even with many advantages, ionizing radiation can generate changes in the material, such as decomposition, the release of toxic agents, and loss of mechanical properties. Therefore, the chemical, physicochemical and mechanical characterization of this material is necessary before and after sterilization, to monitor the properties of the biomaterial.

![Figure 1 – Representative Polyurethane Chain.](image)

**Material and methods**

**Material**

Polymeric material has a numbering: Carbothane PC-85A. The organic solvent used is classified as a class 2 solvent. The mold used for dipping consists in a stainless steel cylinder (patent protect).

**Film manufacture**

Polymer material: Carbothane PC-85A. The organic solvent used is Chloroform (CHCl\(_3\)), which has a molecular mass of 119.38 g mol\(^{-1}\), allowed by the Pharmacopoeia with a concentration limit of 60 ppm, which is classified as a class 2 solvent. The mold used for immersion consists of a stainless steel cylinder. The manufacturing methodology is described in Patent BR 1020180039490.

**Sterilization**

The samples were irradiated in the Cobalt-60 type multipurpose irradiator (CETER, IPEN-CNEN/SP). Red Perspex\textsuperscript{®} polymeric dosimeters (5–50 kGy) were used as dose control. The doses were 15; 25; and 50 kGy. Also subjected to the Hydrogen Peroxide plasma gas (made in Sterrad\textsuperscript{®}) and Ethylene Oxide (EtO).

**Physical and chemical characterization**

**Thermogravimetry (TG)**

The curves of the samples were obtained in the model DTA–60H, Shimadzu brand, belonging to the Prof\textsuperscript{º} Ivo Giolitto Laboratory of the Institute of Chemistry of the University of São Paulo, with Pt crucible, \(\approx 15\) mg, under dynamic air atmosphere (50 mL min\(^{-1}\)), heating rate (\(\beta\)) = 20 °C min\(^{-1}\) and temperature range between 25 and 700 °C.

**Differential exploration calorimetry (DSC)**

The DSC curves of the samples were obtained from the TA Instruments DSC6000 equipment, belonging to the multi–user laboratory of the IPEN Radiation Technology Center, with Pt crucible, \(\approx 5\) mg, under an inert Nitrogen atmosphere (50 mL min\(^{-1}\)).
heating rate ($\beta$) = 10 °C.min$^{-1}$, with first heating at 100 °C, followed by cooling at -30 °C, and a second heating at 250 °C.

**Fourier transform infrared abscess spectroscopy (FTIR)**

The spectra were obtained by an absorption spectrophotometer of the brand BOMEM, model MB102, belonging to Biolab–CIETEC, in the region from 4000 to 400 cm$^{-1}$, with an abscissa represented by the wave number (cm$^{-1}$) and ordered by transmittance (%). The accessory used to evaluate the films was the attenuated total reflectance (ATR) technique with diamond crystal and laser source with inert gas from HeNe. The analyzed films have an average thickness of 0.20 mm.

**Scanning electron microscopy (SEM)**

The images were obtained at the CELAP Lasers and Applications Center (IPEN–CNEN / SP) in a HITACHI TM3000 MEV microscope, Acceleration Voltage: 5 or 15 kV, Tungsten Source, 3000x Magnification with 30 nm Resolution, Integrated EDS. Load reduction mode (with upper chamber pressure) under vacuum, without the need to cover the sample with gold.

The support was covered with carbon tape.

**Optical coherence tomography (OCT)**

The images were obtained at the Lasers and Applications Center – CELAP (IPENCNEN / SP) on the Thorlabs Spectral Radar 930 nm device. The film samples were cut 1x1 cm for reading. The film was extended over a glass slide with stainless steel casting allowing an air/air interface for the film to stick to the glass slide. The grayscale image was performed. The calculation of the optical attenuation coefficient was performed by software (in house) allowing the measurements.

**Results and discussion**

**Fourier transform infrared spectrometry (FTIR)**

The spectrum in the infrared region allows the visualization of the vibrational modes of the chain (Fig.2), the intensity of the band (Tab.1) does not interfere in the composition of the polymer, but in the exposure of its surface area, since the connection involved can be more or less reduced in relation to another sample. It can be seen that even with the treatment and sterilization, the chemical composition of the material remains the same, with no change in the region of the bands or vibrational modes showing that regardless of the sterilization process, the current is not modified. The intensity is related to the dipole moment of the molecule: the greater the dipole moment, the stronger the signal for the characteristic functional group. In this case, the intensity shows the arrangement of the chain, suggesting that the material has not been modified, that is, it has not been degraded, generating monomers or secondary compounds. All samples, therefore, had the same profile in the infrared spectrum. As it is a film made of material protected under patent and considered technological innovation, it is not possible to make a comparative way with the literature, but between them.

**Figure 2** – Spectra in the infrared region for films with different sterilization techniques. a: Standard; b: Plasma; c: Ethylene Oxide; d: 15 kGy; e: 25 kGy; f: 50 kGy.
Table 1 – Results of the Spectra in the infrared region for films with different sterilization techniques.

<table>
<thead>
<tr>
<th>Ligation</th>
<th>vibration</th>
<th>Band</th>
<th>Standard</th>
<th>Plasma</th>
<th>EtO</th>
<th>15kGy</th>
<th>25kGy</th>
<th>50kGy</th>
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<tbody>
<tr>
<td>O=NC=O</td>
<td>−I</td>
<td>1460</td>
<td>89,55</td>
<td>89,42</td>
<td>88,36</td>
<td>86,46</td>
<td>87,22</td>
<td>86,16</td>
</tr>
<tr>
<td>N−H</td>
<td></td>
<td>2930</td>
<td>83,92</td>
<td>80,24</td>
<td>80,09</td>
<td>79,06</td>
<td>79,14</td>
<td>79,43</td>
</tr>
<tr>
<td>N−H</td>
<td>−II</td>
<td>1525</td>
<td>86,82</td>
<td>84,99</td>
<td>84,65</td>
<td>83,05</td>
<td>87,23</td>
<td>87,97</td>
</tr>
<tr>
<td>O=C=O(O)</td>
<td></td>
<td>790</td>
<td>75,60</td>
<td>70,95</td>
<td>70,92</td>
<td>70,07</td>
<td>70,37</td>
<td>69,32</td>
</tr>
<tr>
<td>C−O−C</td>
<td></td>
<td>1012</td>
<td>91,87</td>
<td>89,74</td>
<td>91,16</td>
<td>90,00</td>
<td>99,88</td>
<td>90,24</td>
</tr>
<tr>
<td>C=O</td>
<td></td>
<td>1716</td>
<td>71,74</td>
<td>65,64</td>
<td>67,62</td>
<td>65,25</td>
<td>55,31</td>
<td>63,14</td>
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<tr>
<td>C−H</td>
<td>sp²</td>
<td>2857</td>
<td>90,11</td>
<td>87,52</td>
<td>87,75</td>
<td>87,00</td>
<td>87,05</td>
<td>86,16</td>
</tr>
<tr>
<td>C−H</td>
<td>sp²</td>
<td>1303</td>
<td>91,99</td>
<td>93,17</td>
<td>89,52</td>
<td>88,50</td>
<td>99,27</td>
<td>88,13</td>
</tr>
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Table 2 – Variation of mass and temperature for polyurethane films.

<table>
<thead>
<tr>
<th></th>
<th>Event I</th>
<th></th>
<th>Event II</th>
<th></th>
<th>Residue</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>∆% (mg)</td>
<td>∆T(°C)</td>
<td>∆% (mg)</td>
<td>∆T(°C)</td>
<td>% (mg)</td>
</tr>
<tr>
<td>TPU</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Standard</td>
<td>92,04</td>
<td>373−427</td>
<td>5.69</td>
<td>427−598</td>
<td>2.27</td>
</tr>
<tr>
<td>Plasma</td>
<td>90.60</td>
<td>367−421</td>
<td>8.22</td>
<td>421−591</td>
<td>1.18</td>
</tr>
<tr>
<td>EtO</td>
<td>91.47</td>
<td>368−423</td>
<td>7.29</td>
<td>423−591</td>
<td>1.24</td>
</tr>
<tr>
<td>15 kGy</td>
<td>92.37</td>
<td>373−425</td>
<td>6.58</td>
<td>425−568</td>
<td>1.05</td>
</tr>
<tr>
<td>25 kGy</td>
<td>91.34</td>
<td>373−426</td>
<td>6.88</td>
<td>426−590</td>
<td>1.78</td>
</tr>
<tr>
<td>50 kGy</td>
<td>92.26</td>
<td>378−423</td>
<td>6.37</td>
<td>423−595</td>
<td>1.36</td>
</tr>
</tbody>
</table>

Thermal analysis
Thermogravimetry (TG)

The thermogravimetry (TG) technique allows to evaluate the thermal behavior of the samples of interest. Fig.3 shows the TG curves of the thermoplastic polyurethane films. It was possible to visualize two events in which the mass variation characterized by thermal decomposition of the material occurs. In all samples, the first decomposition event presents the largest mass variation, almost the totality of the sample. In the second event, it presents a smaller mass variation. A small residual mass content was observed with respect to the material added in the pellet composition, or BaSO₄.

Comparatively it should be noted that the similarity between the TG curves can be considered equivalent, presenting discrete differences in relation to the thermal stability of the studied material. Based on the evaluation of these results shown in Tab.1, it is possible to conclude that, in this case, the plasma sterilized sample presents lower thermal stability in relation to the other techniques. The samples sterilized by ionizing radiation have a profile very similar to the standard sample. All samples presented the same thermal profile, showing only different residual contents and discrete variation in temperature ranges.

Differential exploratory calorimetry (DSC)

In the DSC curves, the physical and chemical events (enthalpic events) that occur in the sample when subjected to heating are observed. In Fig.3 the DSC curves performed for the films are shown in a comparative way. In this way it is possible to analyze the similar thermal behavior with the same number of events in close temperature intervals, corroborating the study carried out in thermogravimetry.

In the first heating, the first point to be observed is the glass transition temperature of the material, which in all samples have similar ranges as described in Tab. 2. In the second heating, the transition is shifted to larger values due to the strengthening of the cross–links where the energy necessary for the chain to undergo the physical order modification will be greater for the transitions.

As with thermogravimetry, plasma sterilized film showed higher thermal stability, even with a minimal difference from the others, whereas radiation sterilized samples showed stability values close to the standard film, this is caused by intermolecular chain forces. Polymeric materials that prevent their displacement, they are weakened when the material is heated, thus allowing the transition of molecules. The fusion event occurs together with the first thermal decomposition event, where the material undergoes physical and chemical changes. At this point, the energy of the system will reach the level necessary to overcome the secondary intermolecular forces between the crystalline phase chains of the polymer, changing from rubberized to fused state, almost total decomposition of the material (98 to 99%).
Figure 3 – DSC curves for polyurethane films with different sterilization techniques.

Table 2 – Vitro transition temperature for polyurethane films sterilized by different techniques.

<table>
<thead>
<tr>
<th>Sample</th>
<th>I Event (°C)</th>
<th>II Event (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TPU Standard</td>
<td>77.71</td>
<td>118.37</td>
</tr>
<tr>
<td>TPU Plasma</td>
<td>71.00</td>
<td>101.13</td>
</tr>
<tr>
<td>TPU EtO</td>
<td>81.69</td>
<td>111.37</td>
</tr>
<tr>
<td>TPU 15 kGy</td>
<td>77.00</td>
<td>110.68</td>
</tr>
<tr>
<td>TPU 25 kGy</td>
<td>78.35</td>
<td>115.69</td>
</tr>
<tr>
<td>TPU 50 kGy</td>
<td>78.71</td>
<td>112.38</td>
</tr>
</tbody>
</table>
Scanning electron microscope (SEM)
Films submitted to sterilization by plasma, ethylene oxide and 15 kGy retained their amorphous surface characteristics as shown in Fig.4, and suggest no modification, while the 25 kGy and 50 kGy treated samples show the surface of the “aged” polymeric film with more evident fibers (arrows in the Fig.4) indicating a possible defect that should be studied through other techniques to corroborate its outcome.

Figure 4 – Scanning electron microscopy images for polyurethane films, arrows indicate regions with superficial change. a: 15 kGy; b: 25 kGy; c: 50 kGy; d: Plasma; e: Ethylene Oxide; f: standard.
Optical coherence tomography (OCT)

All films presented the same profile, only the 50 kGy dose gamma-irradiated film showed irregularities perpendicular to the edges (arrows in the Fig. 5), indicating that the material may be degrading or losing some property.

Figure 5– Figures obtained by optical coherence tomography for polyurethane films, arrows indicate regions with characteristic changes. a: Standard; b: Plasma; c: Ethylene Oxide; d: 15 kGy; e: 25 kGy; f: 50 kGy.

Conclusion

The present work has as main objective to study the influence that ionizing radiation can cause in films made of thermoplastic polyurethane.

Manufacturing should be performed at controlled temperature and humidity to ensure reproducibility of material thickness and intrinsic characteristics. Thermogravimetry and differential calorimetry showed that the sterilization technique interferes with the thermal stability of the films, even slightly, making the material sterilized by plasma and ethylene oxide less thermally stable, whereas those sterilized by ionizing radiation maintained the characteristics of the film without sterilization. The image characterization techniques were important for the verification of superficial changes, noting a slight modification regarding the radiation sterilization technique. Using the techniques in a complementary way it is possible to conclude that the material does not undergo significant modifications for the purpose of the study, thus maintaining the characteristics of the standard material.

Acknowledgment

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References


