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THERMOPLASTIC POLYURETHANE AS BIOMATERIAL - STUDY OF THE MODIFICATION CAUSED BY IONIZING RADIATION

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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 physicochemical 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) and FTIR-ATR (Fourier Transform Infrared Spectrometry) have proved that the material, after applied the sterilization techniques, maintains its physical-chemical characteristics and does not suffer any modifications after the treatment.

1. 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 2005[1]. 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 world [2]. 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 in genera. Supposedly, this market will continue to be led by North America, Europe and Asia over the next few years [3].

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 diseases [4].

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 lining [6].

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 complications [7].

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 characteristics [8].

Polyurethanes are formed from the reaction of diisocyanates and polyolefins 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 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 [9].

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 [10].

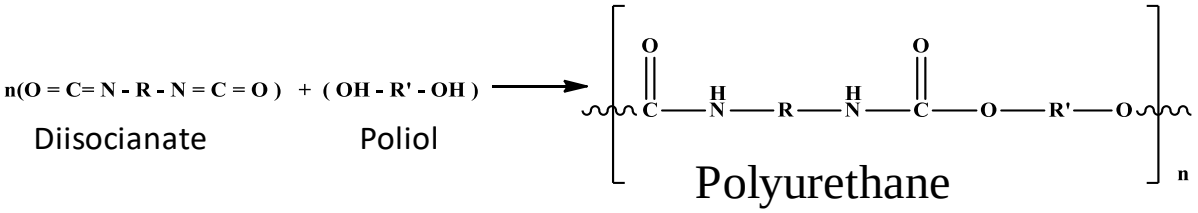

Figure 1: Representative Polyurethane Chain.

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 [11]. 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 [12].

Even with many advantages, ionizing radiation can generate changes in the material, such as is 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.

2.0 MATERIAL

Polymeric material has a numbering: 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 dipping consists in a stainless steel cylinder.

3.0 METHODS

3.1 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 dipping consists in a stainless steel cylinder.

3.2 Sterilization

The samples were irradiated in the Cobalt-60 type multipurpose irradiator (CETER, IPEN-CNEN/SP). Red Perspex® 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®) and Ethylene Oxide (EtO).

4.0 CHARACTERIZATION

4.1 Thermogravimetry / derivative thermogravimetry (TG)

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

4.2 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, ≈ 5 mg, under an inert Nitrogen atmosphere (50 mL.min^{-1}), heating rate (β) = 10 °C.min $^{-1}$, with first heating at 100 °C, followed by cooling at -30 °C, and a second heating at 250 °C.

4.3 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 of 4000 to 400 cm^{-1}, with abscissa represented by wave number (cm^{-1}) and ordered by transmittance (%). The analyzed films have an average thickness of 0.20 mm.

5.0 RESULTS

5.1 FTIR

The spectrum in the infrared region allows the visualization of the vibrational modes of the chain (Fig. 2), the intensity of the band does not interfere in the composition of the polymer, but in the exposure of its surface area, since the involved connection can be more or less collapsed in relation to another sample. It can be verified that even with the treatment and sterilization, the chemical composition of the material remains the same, without alteration in the region of the bands or vibrational modes showing that regardless of the sterilization process, the chain is not modified.

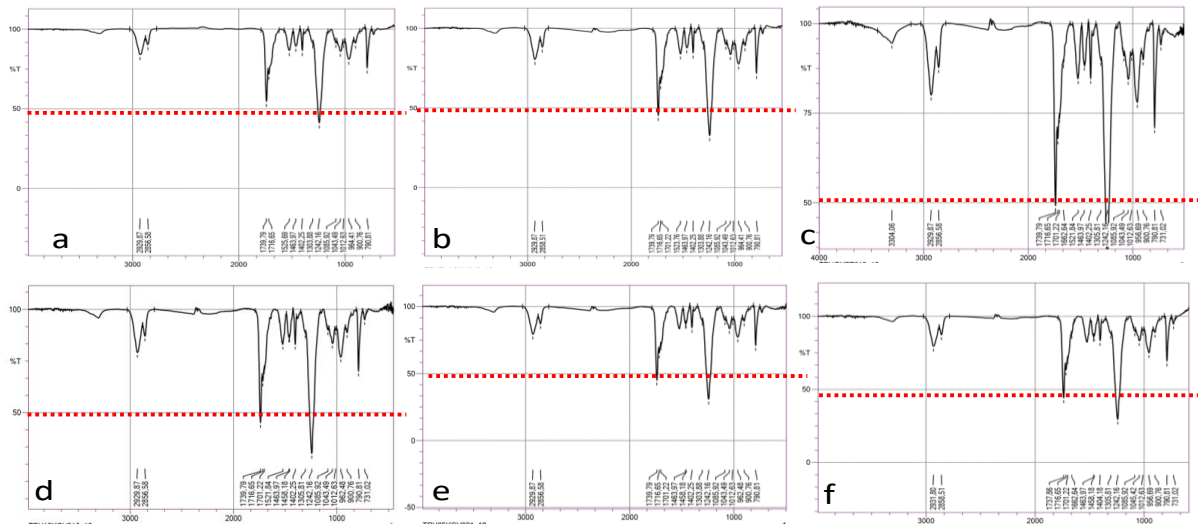

Figure 2: Spectra in the infrared region for films with different sterilization techniques. a: Standard; b: Plasma; c: Ethylene Oxide; d: 15 kGy; e: 25 kGy; f: 50 kGy.

We can observe similar profiles in the obtained spectra, suggesting that the material did not undergo chemical modifications with the sterilization. The spatial arrangement of the polymer chain can interact with the Infrared beam in a more intense manner as shown, for example, with ethylene oxide and 15 kGy sterilization. The intensity is related to the dipole moment of the molecule: the higher the dipole moment, the stronger the signal for the characteristic functional group. In this case the intensity demonstrates the arrangement of the chain suggesting that the material did not undergo modifications, that is, it was not degraded generating monomers or secondary compounds. All samples therefore had the same profile in the infrared spectrum.

5.2 THERMAL ANALYSIS

5.2.1 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 $BaSO_4$.

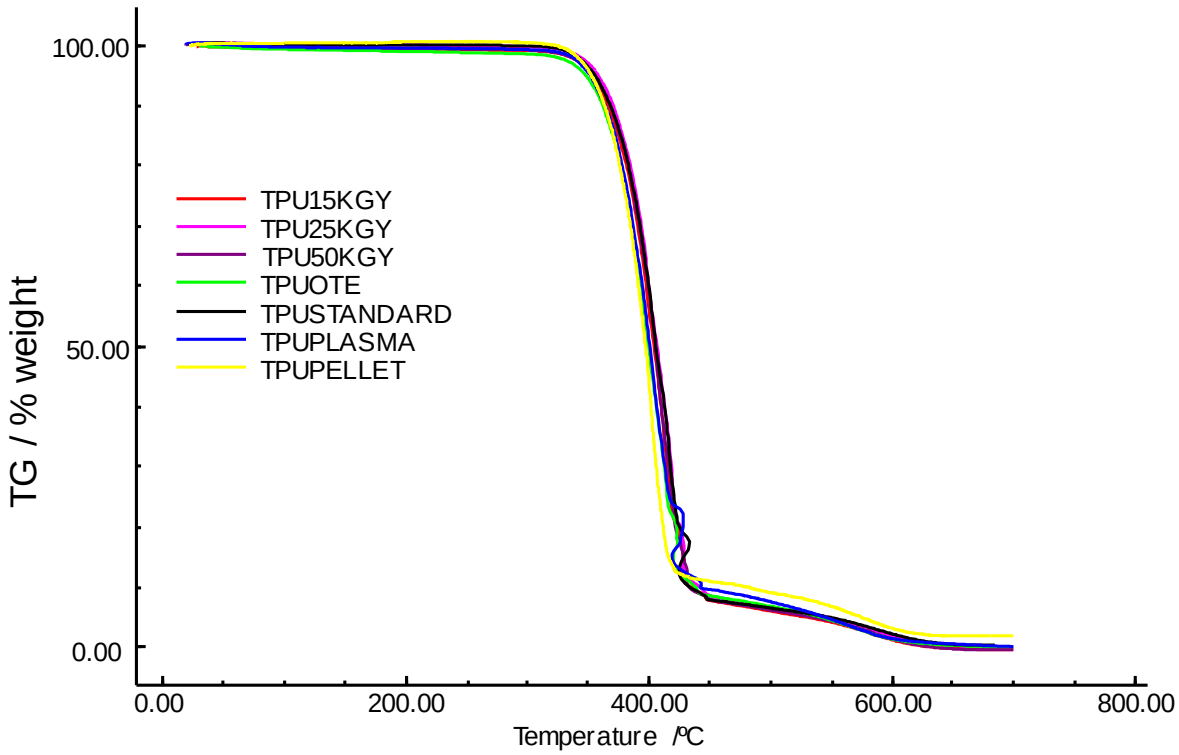

Figure 3: TG curves of polyurethane films with different sterilization techniques

Table 1: **Variation of mass and temperature for polyurethane films**

	Event I		Event II		Residue
TPU	**Δ% (mg)**	**ΔT(ºC)**	**Δ% (mg)**	**ΔT(ºC)**	**% (mg)**
Standard	**92.04**	**373-427**	**5.69**	**427-598**	**2.27**
Plasma	**90.60**	**367-421**	**8.22**	**421-591**	**1.18**
EtO	**91.47**	**368-423**	**7.29**	**423-591**	**1.24**
15 kGy	**92.37**	**373-425**	**6.58**	**425-588**	**1.05**
25 kGy	**91.34**	**373-426**	**6.88**	**426-590**	**1.78**
50 kGy	**92.264**	**378-423**	**6.37**	**423-595**	**1.36**

Comparatively, the TG curves of the samples (Fig. 3) show the characteristics and the thermal profile of the samples. It should be noted that the similarity between the 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

5.2.2 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.4 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.

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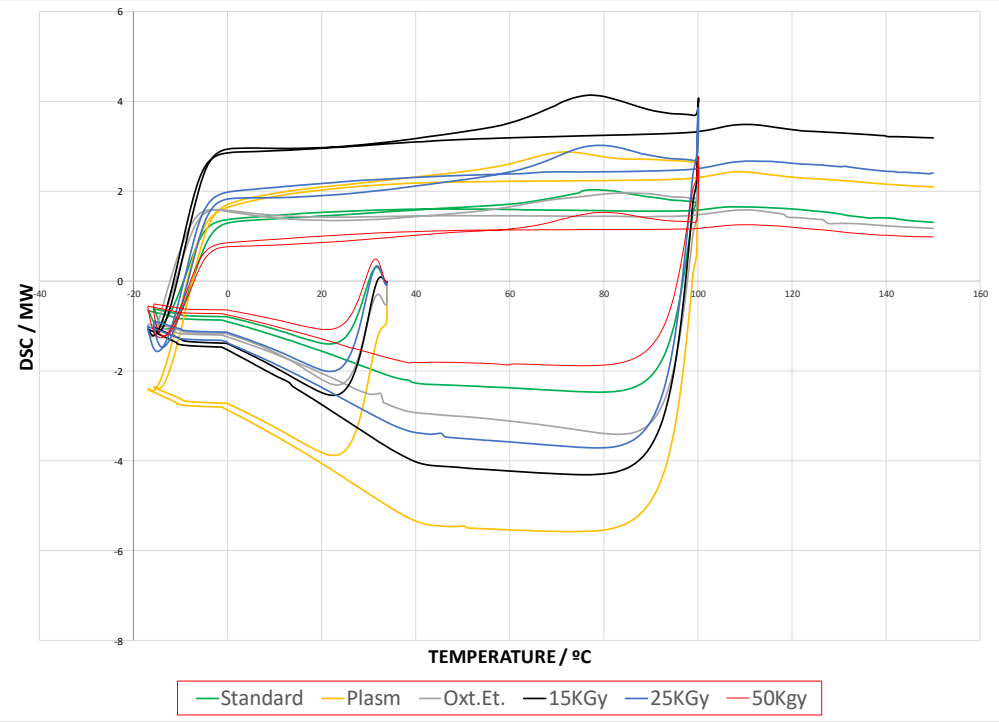

Figure.4. DSC curves for polyurethane films with different sterilization techniques

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.

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

Sample	I Event (ºC)	II Event(ºC)
TPU Standard	77.71	118.37
TPU Plasma	71.00	101.13
TPU EtO	81.69	111.37
TPU 15 kGy	77.00	110.68
TPU 25 kGy	78.35	115.69
TPU 50 kGy	78.71	112.38

As in Thermogravimetry, the plasma sterilized film presented higher thermal stability. even if by a minimum difference in relation to the others, while the samples sterilized by radiation had values close to the standard film. The intermolecular forces of the polymer chains prevent their displacement, which are weakened when the material is heated, thus allowing the transition of the molecules. The fusion event occurs along with the first thermal decomposition event, where the material undergoes physical and chemical change. At this point, the energy of the system will reach the level required to overcome the secondary intermolecular forces between the chains of the crystalline phase of the polymer. This explanation differs from ionic materials, because in this case the chain will lose its regular packaging structure, changing from the rubbery to molten state, decomposing the material almost entirely (98 to 99%).

6.0 CONCLUSION

The present work has the main objective of studying the influence that the ionizing radiation can cause in films constituted by thermoplastic polyurethane. Manufacturing must have controlled temperature and humidity, ensuring the reproducibility of the thickness and intrinsic characteristics of the material. After sterilization, the study of possible physical and chemical modifications required complementary techniques to verify that the material does not undergo significant modifications. Thermogravimetry and differential scanning calorimetry showed that the sterilization technique interferes in the thermal stability of the films, even though in a discrete manner, rendering the material sterilized by Plasma and Ethylene Oxide less thermally stable, whereas those sterilized by ionizing radiation maintained its characteristics.

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