Sterilize Polylactic Acid

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1. Overview

How sterilization techniques accurately affect the properties of biopolymers continues to be an issue of discussion in the field of biomedical engineering, particularly now with the development of 3D-printed devices. One of the most widely used biopolymers in the manufacture of biomedical devices is the polylactic acid (PLA). Despite the large number of studies found in the literature on PLA devices, relatively few papers focus on the effects of sterilization treatments on its properties. It is well documented in the literature that conventional sterilization techniques, such as heat, gamma irradiation and ethylene oxide, can induced damages, alterations or toxic products release, due to the thermal and hydrolytical sensitivity of PLA. The purposes of this paper are, therefore, to review the published data on the most common techniques used to sterilize PLA medical devices and to analyse how they are affecting their physicochemical and biocompatible properties. Emerging and alternative sterilization methods for sensitive biomaterials are also presented.

2. Sterilization

Sterilization is an important and problematic step that should be considered as early as possible in the design of any new medical device intended to be use in contact with sterile tissues, mucous membranes, or breached skin, in order to save money, time and trouble [1]. Any failure associated with the sterilization could trigger significant institutional costs related to disease transmission in a bad reuse or with the appearance of nosocomial infections in patients. Thanks to advances in device sterilization methods, fortunately, most nosocomial infections today are not related to this issue. However, it is important to consider sterilization issues and requirements at the earliest stages of the development of any new medical device, to ensure that the final product can be sterilized in an effective and safe manner, with the most cost-effective and environmentally friendly procedures [1]. The vast majority of traditional biomedical devices were designed to withstand traditional sterilization techniques. However, with advances in regenerative medicine and tissue engineering, we can say that we are dealing with a new generation of biomedical biomaterials, much more complex and even patient-specific, thanks to 3D printing. The importance of sterilization or elimination of pathogens has become very relevant nowadays, creating a great social awareness due to the COVID-19 crisis.

Despite this important step after the manufacture of any biomedical device only two studies have been found that compared more than two sterilization methods for PLA, analysing both physicochemical and biocompatibility changes [2][3]. Since PLA is a thermal and hydrolytic sensitive biomaterial, conventional sterilization techniques such as heat sterilization, gamma irradiation, and ethylene oxide, may not be the ideal methods for sterilization of PLA. It can be concluded that saturated steam heat (autoclave) is discarded by most authors causing complete deformations and profound structural changes. Although gamma irradiation causes molecular weight changes and chain scissions among others, these changes were considered by most authors as not significant and not affecting biocompatibility, thus accepting this method in many cases. Ethylene oxide also produced some changes in PLA, but although its major problem is toxicity and residues, some authors demonstrated the biocompatibility of the materials after sterilization with this method. Other techniques such as E-beam and HPGP have also been described to sterilize PLA effectively without producing severe changes. E-beam produces less degradation than gamma irradiation, but the penetrating power is dependent on the kinetic energy and the density of the biomaterial, causing more damage as the energy increases. The

HPGP sterilization seems to be a promising technique for many authors. However, some authors do not recommend gas plasma as a sterilization method for surgical guides and PLA biomodels with voids as complete sterilization was not achieved. Its lower penetration depth compared to other techniques may be the reason why it is most used as a surface sterilization technique for implantable devices and polymers.

The new $scCO_2$ sterilization technique is strongly emerging as an effective technique for the sterilization of sensitive materials. Despite the fact that this technique has taken its first steps in some regulatory agencies, it is necessary to study this technique in detail, to guarantee a correct sterilization and preservation of the bio functionality of the materials, at the same time. Parameters such as pressure, temperature, time, and the use of additives are key for a regulation of the methodology and standardization.

Recently, some authors were also discussing the 3D printing process as a self-sterilization technique, although all biomodels or scaffolds still need to undergo a sterilization process before being used in an operating room to avoid risks of contamination during the manufacturing process and especially if the working environment is not completely sterile. In the specific case of 3D-printed devices, special care must be taken because they are usually hollow. As detailed by Aguado-Maestro [4], it is very important that sterilization is also effective inside the voids in case that a model breaks during a surgical intervention. This is the first publication regarding the sterilization methods of in-hospital manufactured 3D-printed biomodels in polylactic acid, but a more in-depth study would be needed in which physical-chemical and biological changes are analysed with more techniques and not only in terms of deformation and sterilization.

Although promising new techniques such as supercritical CO_2 have emerged, much needs to be done to expand knowledge regarding sterilization methods for sensitive materials. Research related to new sterilization methods is also required, that address many of the limitations of current techniques, where many single-use biomedical devices can be reused, with clear economic benefits. The effectiveness and post-sterilization effects of new emerging techniques need therefore to be further investigated before they can be declared safe and effective for their use.

3. Conclusions

PLA is a widely used biomaterial for the processing of implantable devices, scaffolds, instruments, guides, or models. Since these devices will be in direct contact with the human body, it is a critical task to choose the appropriate technique to effectively sterilize but at the same time to maintain structural and physicochemical integrity, without compromising the biocompatibility.

This paper aims to help researchers to choose the best sterilization method and better understand the changes related to PLA. It is clear, that no suitable “perfect sterilization technique” for PLA exists and the choice should be based on the type of product to be sterilised and the applications for which it will be manufactured as well as the best available techniques in each case and each moment. A thorough analysis of the changes should always be made to avoid compromising their function. Moreover, the operation conditions of a chosen sterilization technique should be precisely controlled and evaluated case by case.

It can be concluded that autoclave is discarded by most authors, except in 3D printing, which seems to be gaining relevance. Ionising radiation (gamma radiation and electron beam) can be effective as long as the dose is controlled to avoid severe changes. The HPGP and new $scCO_2$ seem to be promising sterilization techniques. In addition, more studies are needed to evaluate the changes produced by the sterilization process especially in novel and sensitive biomaterials. As for 3D printing, this technique must also be provided with the necessary protocols and validation so that its use in hospitals can be applied easily, safely, comfortably, and universally.

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