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Review

# Impact of sterilization methods on electrospun scaffolds for tissue engineering

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ABSTRACT

Tissue engineering is a growing area within the regenerative medicine. The electrospun scaffolds are the most promising devices for translating engineered tissues into patients. However, in order to be used in clinical practice, one of the important fundamental aspects of the scaffold is to be sterile keeping the fact of patient safety in mind. Due to the various properties of electrospun fibers, such as high porosity and surface area, the effects of sterilization could have different outcomes than those observed in ordinary medical devices. Therefore, the present article provides an insight into the various sterilization methods that have been applied to electrospun scaffolds and their effects on scaffolds morphology, hydrophilicity, other physico-chemical and mechanical properties and the performance of seeded cells after sterilization. In conclusion, the information provided in the review will help all scientists involved in this interdisciplinary field to understand and apply the knowledge in selection of appropriate sterilization method for the electrospun scaffolds.



**Contents**



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## 1. Introduction

Tissue engineering is a rapidly growing area in regenerative medicine and the development of scaffolds to support cell growth *in vitro* and/or *in vivo* is the objective of many researchers worldwide. Electrospun scaffolds mimics the natural fibers present in the extracellular matrix and has been shown to provide appropriate cues for cell proliferation, differentiation and survival [1–6].

Synthetic and natural derived polymers can be used in electrospinning processes. The advantages of natural polymers refer to their better biocompatibility, lower immunogenicity, and higher capacity of evoking cell signaling, which is very important in tissue regeneration. However, mechanical properties, degradation rate and reproducibility are some downsides of the natural polymers. On the other hand, synthetic polymers can be modified to reach the desired properties; they have better batch to batch uniformity, and are cheaper than natural polymers [7–9]. Over a hundred polymers have been electrospun, but the most commonly applied for tissue engineering purposes are the polyvinyl alcohol (PVA), poly ethylene oxide (PEO), poly lactic acid (PLA) and its polymeric isomers (poly-L-lactide PLLA and poly-D-lactide PDLA) and copolymer poly(L-lactide-co-D,L-lactide) (PLDLLA), poly lactic co-glycolic acid (PLGA), poly caprolactone (PCL), chitosan, alginate, collagen, gelatin, hyaluronic acid, and silk [10,11]. In the present manuscript, we have discussed some of the relevant polymers involved.

A critical attribute of implantable medical devices is their sterility. Every implantable medical device, such as scaffolds for tissue engineering must be sterile in order to be applied on a patient, i.e., it must be absent of viable microorganisms. Sterile medical devices are obtained by either aseptic fabrication or terminal sterilization. However, terminal sterilization is preferred over aseptic processing, being the later option accepted only when the first one is not feasible [12–15]. It is important to highlight that treatments with ethanol solutions and/or UV radiation are not approved as sterilization methods by health authorities and are correctly classified as disinfection methods. The Center for Disease Control defines sterilization as a process that destroys or eliminates all forms of microbial life, while disinfection describes a process which eliminates many or all pathogenic microorganisms, except bacterial spores, on inanimate objects [16].

Sterilization methods described in recognized pharmacopoeias either remove microorganisms (filtration of liquids and gases) or inactivate the microorganisms (physical or chemical methods), being only the later appropriate approaches for electrospun scaffolds. Examples of physical inactivation methods are dry or wet heat (which are the most commonly used) and irradiation, while chemical inactivation methods include treatment with hypochlorite solution, hydrogen peroxide vapor, ethylene oxide gas, and ozone [17,18].

Regardless the sterilization method, validation is required to ensure the efficacy of the method when applied to different kinds of materials and loads to be processed. Physical measurements and biological indicators should demonstrate the efficacy of sterilization methods, and the sterility tests are the means of verifying the sterility of the sterilized products [13,18].

Other than qualifying the sterility test, the sterilization method should be innocuous to the medical device and not cause any deleterious effects on its morphology, physico-chemical properties or biological performance. The main attributes of electrospun fibers are the presence of high porosity and high surface area, especially nanofibers; consequently, the effects of sterilization could have different outcomes than those observed in other forms of the same materials, as observed by Phillip et al. [19]. Therefore, many researchers have evaluated the effects of sterilization methods on electrospun scaffolds [20–26]. Such scaffolds subject to sterilization were made of polymers, most of them polyesters, and normally characterized for their physicochemical properties, morphology, or cell behavior after the sterilization process. This review is emphasized on the sterilization of electrospun scaffolds, the methods that have been employed so far, as well as their impact on the sterilized polymeric fibers. We have discussed the conventional sterilization methods followed by the disinfection methods routinely used in the lab along with various recent techniques.