Macedonian pharmaceutical bulletin, 69 (Suppl 1) 55- 56 (2023)
Online ISSN 1857 - 8969
DOI: 10.33320/maced.pharm.bull.2023.69.03.027
Short communication

Electrospun nanofibers as potential medical devices: Short review from a regulatory perspective

Luca Éva Uhljar*, Ildikó Csóka, Rita Ambrus

Institute of Pharmaceutical Technology and Regulatory Affairs, University of Szeged, Eötvös Street 6, H-6720 Szeged, Hungary

Introduction

Nanotechnology is a dominant innovative technology in many of today's industries. In the pharmaceutical and healthcare sectors, nanotechnology-related R&D is also on the rise. There is a mass of scientific publications on the subject and, in addition to basic research, it is constantly becoming the focus of applied research, as well.

One tiny part of the whole nanotechnology topic is the polymer-based nanofibers. The nanofibers have many advantages that can be beneficial in several areas of biomedicine. Therefore, there is a very wide range of electrospun nanofibers in the biomedical field with applications varied from drug delivery systems to tissue engineering scaffolds and soft electronics.

In this short review, the aim was to provide an overview of the regulation of medical devices and specially nanofibers that can be used as medical devices.

Materials and methods

For data collection, the scientific literature and WHO, FDA and EMA guidelines were reviewed.

Results and discussion

Regulation of medical devices

Definition of medical devices: A global definition of medical devices is difficult to create because there are various regulatory agencies worldwide that regulate the marketing of medical devices. Although these agencies frequently communicate and discuss the harmonization, the accepted definition of a medical device varies regionally. According to the World Health Organization, the definition is the following. "A medical device can be any instrument, apparatus, implement, machine, appliance, implant, reagent for in vitro use, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination for a medical purpose. Typically, the purpose of a medical device is not achieved by pharmacological, immunological or metabolic means" (WHO, 2017). So, medical devices and medicines can be distinguished from each other based on whether they contain an active substance or not.

Classification of medical devices: Like the definition, the classification of medical devices also depends on the region. However, all of them are based on the level of control required to assure the safety and effectiveness of the device. There are usually three or four classes, where the first class representing the lowest-risk devices. The higher the category of the instrument, the regulation is stricter and requires more studies. Usually, before the highest category of devices can be authorized, clinical trials must be carried out.

Challenges of nanotechnology-based medical devices: Even though the regulation regarding conventional medical devices is strict and thoroughly managed; in the case of nanotechnology-based devices, it has not yet been clearly defined. The regulation of nanomedicine is not clear, and the number of specific regulatory guidance is poor. Recently, there are signs of improvement, for example, the FDA published guidance titled "Drug Products, Including Biological Products, that Contain Nanomaterials – Guidance for Industry". However, it does not deal with medical devices.

In general, the agencies are more careful with nanomaterials and the producers must fulfill extra

*uhljar.luca.eva@szte.hu

requirements. For example, in the EU, Special Rule 19 applies to all nanomaterial-associated devices, regardless of their classification.

Electrospun nanofibers as medical devices

A large group of electrospun nanofibers developed for biomedical use has the potential to become a future medical device. Some of these belong to the higher-risk classes, such as tissue engineering scaffolds or stent coatings. The other part is not implanted, so it has a less prominent contact with the human body and belongs to the class I. One typical group of the latter is nanofibrous filters in protective clothing.

Three different groups of electrospun medical devices are described below (Uhljar, 2023).

Wound dressings: Nanofiber dressings have great potential for chronic wound management because they have most of the properties of an ideal dressing, such as protection against bacteria and external aggression, absorption of excess exudates, adequate gas exchange, providing a moist environment, being painless for the patient, and being easily removable. Moreover, electrospun nanofibers can mimic the extracellular matrix, regulate skin cell responses including proliferation, migration, and differentiation, and thus reduce wound healing time. So, non-healing chronic wounds (e.g., diabetic ulcers) can be closed faster.

Nanofibers can be loaded with various APIs which puts them in the grey zone between medicines and medical devices. It is worth noting that the EMA has created a group dedicated to "Borderline products" and gave the national competent authorities the choice to decide between the two categories. In the case of wound dressings, the incorporation of different molecules or nanoparticles, such as antibacterial agents against infections or growth factors for faster tissue regeneration, can be beneficial.

Tissue engineering scaffolds: In general, nanofiber scaffolds have several beneficial properties to provide adequate tissue replacement, such as high porosity, large surface area, biodegradability, biocompatibility, and tailorable 3D architecture. They can provide excellent support for cell adhesion, proliferation, and differentiation due to their ability to mimic the required extracellular matrix in biological and mechanical features such as alignment, nano-topography, stiffness, and tensile strength. By choosing the right method of electrospinning, similar structures to the original tissue can be achieved.

These scaffolds will be implanted in the human body, so they will certainly belong to the highest class of medical devices. For this reason, they require both non-clinical and clinical verification, for which of course GLP and GCP adherence is essential. Besides data quality and integrity requirements, ethical standards are also important elements of the GCP.

Protective clothing: Nanofibers are very effective as filters due to their large specific surface area and adjustable pore size. As an element of protective clothing, face masks have recently received particular attention due to the COVID-19 pandemic. Several publications have reported the excellent protective properties of nanofibrous masks.

The authorization procedure got quicker as the authorities, for example, the FDA in March 2020, issued emergency use authorizations for personal respiratory protective devices. Two things should be highlighted regarding this. First, the emergency use authorization procedure did not mean fewer criteria or poorer quality. Second, these items are in the low-risk class, so in most cases there is no obligation of pre-market authorization but only a notification.

Conclusion

The regulation of medical devices, as substances and items used to maintain and restore health, is receiving particular attention worldwide. The countries' national agencies and the World Health Organization have their own definitions, classification, and guidelines. However, in our globalized world, countries are more and more interconnected and there is a need for common, harmonized terminology and regulation.

The field of nanomaterials is particularly challenging as the regulation of nanomaterials is still evolving. Electrospun nanofibers belong to nanomaterials because of their nano-sized diameter. It is agreed that extra caution is necessary in the case of nanomaterial-containing medical devices, and they shall be classified into higher-risk categories. These should be kept in the eye when planning the R&D of electrospun medical devices.

Acknowledgements: This research was funded by Gedeon Richter Plc. Centennial Foundation.

References

Uhljar, L.É., Ambrus, R., 2023. Electrospinning of Potential Medical Devices (Wound Dressings, Tissue Engineering Scaffolds, Face Masks) and Their Regulatory Approach. Pharmaceutics. 15, 417. doi: https://doi.org/10.3390/pharmaceutics15020417

World Health Organization. 2017. Global Atlas of Medical Devices; WHO Medical device technical series; World Health Organization: Geneva