TOPICAL NITRIC OXIDE-RELEASING POLYETHYLENE TEREPTHALATE MESH INCREASES DERMAL VASODILATION


Abstract
The topical application of nitric oxide-releasing biomaterials has shown to be effective for promoting the increase of dermal vasodilation and wound healing. The main aims of this work are the development of a new platform for topical NO release, based on polyethylene terephthalate (PET) meshes impregnated with a NO-releasing polynitrosated polyester (PNPE) and the correlation of the kinetics of NO release in vitro with the dermal vasodilation in vivo. The polyester meshes were obtained from Band-aid® bandages. The PNPE was synthesized through the polycondensation reaction between a diol and a sulfhydrylated diacid, generating a polysulfhydrylated polyester (PSPE).

Key words: Biomaterials, Nitric oxide, Vasodilation

Introduction
Nitric oxide (NO) is produced by a wide variety of cell types and displays multiple biological actions, including the relaxation of smooth muscle cells, leading to vasodilation, the modulation of the immune response and neurotransmission\(^1\). Since the discovery of the biological properties of NO, there has been a growing interest in formulations and biomaterials capable of releasing NO in a controlled manner\(^2,3\).

The main aim of this work is the preparation of polyethylene terephthalate (PET) meshes impregnated with a NO-releasing polynitrosated polyester (PNPE), and the characterization of the correlation between the NO doses and the dermal vasodilation obtained in topical applications of the PET/PNPE meshes in the healthy skin of human volunteers. PET meshes were impregnated with PNPE from acetone solutions of the sulfhydrylated polymer to obtain PET/PNPE meshes containing 5, 15 and 25 wt% of PNPE. The morphology of the PET/PNPE meshes was characterized by optical microscopy. The doses of NO were measured by chemiluminescence and the dermal vasodilation was measured by laser Doppler flowmetry.

Results and Discussion

The optical microographies of Fig. 1 show that the impregnation process with 5, 15 and 25 wt% of PSPE lead to an increasing amount of PSPE deposited in the interfibrilar spaces, while preserving the porosity of the meshes.

![Fig. 1. Optical micrographs of native PET/PSPE mesh (a), PET/PSPE 5 wt % (b), PET/PSPE 15 wt % (c) and PET/PSPE 25 wt % (d), before nitrosation.](image)

![Fig. 2. (A) Amount of NO released from PET/PNPE meshes containing 5, 15 and 25 wt% of PNPE. (B) Laser Doppler measurements of dermal vasodilation obtained in topical applications PET/PNPE meshes on the forearm of volunteers.](image)

The dose of NO thermally released from the PET/PNPE meshes in the range of 30-130 \(\mu\)mol/g, is directly proportional to the wt% of PNPE (Fig. 2 A). PET/PNPE meshes 15 and 25 wt % led to a 12-fold increase in the dermal vasodilation, compared to a 3-fold increase obtained with the PET/PNPE 5 wt%, relative to the basal level (Fig. 2 B).

Conclusions
Impregnation of PET meshes with NO-releasing PNPE led to a new platform with potential applications for the topical treatment of impaired dermal vasodilation.

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