

## TOPICAL NITRIC OXIDE-RELEASING POLYETHYLENE TEREPHTHALATE MESH INCREASES DERMAL VASODILATION

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### 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

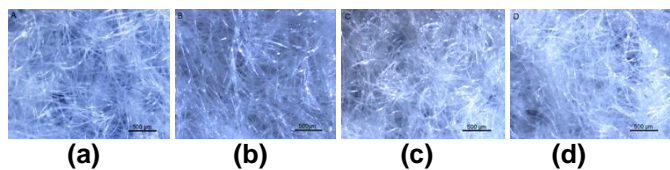
### Introduction

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<sup>1</sup>. 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<sup>2,3</sup>.

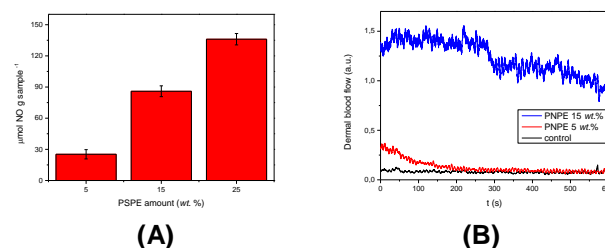
The main aim of this work is the preparation of poly(ethylene terephthalate (PET) meshes impregnated with a NO-releasing polynitrosated polyester (PNPE), and the characterization of the correlation between the NO doses and the dermal vasodilation obtained in topical applications of the PET/PNPE meshes in the healthy skin of human volunteers. PET meshes were impregnated with PNPE from acetone solutions of the sulphhydrylated 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 micrographies 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 interfibrillar spaces, while preserving the porosity of the meshes.



**Fig. 1.** Optical micrographies of native PET/PSPE mesh (a), PET/PSPE 5 wt % (b), PET/PSPE 15 wt % (c) and PET/PSPE 25 wt % (d), before nitrosation.



**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.

The dose of NO thermally released from the PET/PNPE meshes in the range of 30-130 µmol/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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