Development of biomimetic tympanic membrane substitutes for the treatment of chronic perforations

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BACKGROUND

Perforation of the tympanic membrane (PTM) is a common cause of consultation in Otolaryngology, due to infections or trauma. The rate of recovery from perforation depends mainly on the size of the perforation and the secondary infections developed. Although **most PTMs heal spontaneously**, **complications** in healing can **lead to a chronic defect**. As a consequence, the chronicity of PTM causes a number of problems for the affected patient such as partial hearing loss.

The **traditional technique** used in the treatment of PTM, known as **myringoplasty,** uses temporalis muscle fascia or tragal cartilage for closure of PTMs, with its **associated morbidity and cost.** Thus, there is growing **interest in the development and application of biocompatible materials as a scaffold for regeneration.**

OBJECTIVES

The **overall objective** is the **development and validation of biomaterials** for the manufacture of scaffolds to be **used as biomimetic tympanic membrane substitutes**. To this end, the **specific goals** are:

1- Development of protein-based biomaterials, optimization of the formulations and evaluation of the structure and properties of the scaffold.

2- Design of a tympanic tissue replacement model to be useful as a scaffold in PTMs.

3- Evaluation of the integration, regeneration and functionality of the substitute in a PTM rat model.

A LOOK AT SOME DATA

Intrinsic properties

WU	WVTR	DR
%	$g/(m^2 day)$	Months
96.4 ± 5.1	1408.0 ± 13.2	>6

Table 1. Evaluation of the water uptake (WU), water vapour transmission rate (WVTR) and degradation degree (DR) of the scaffold. For the latter, it was exposed to water and "simulated body fluid" for 6 months.

The substitute showed adequate hydration and permeability properties, and did not degrade when exposed to water long term.

Functional properties

Pressure resistance	Adhesion capacity
kg	*g*
4.1 ± 0.2	5.4 ± 0.4

Table 2. Determination of the functional properties performed in a texturometer (Ta. XTplus Texture Analyser - Stable Micro System). In order to assess the pressure resistance and adhesion capacity, puncture test and mucoadhesion test were applied respectively.

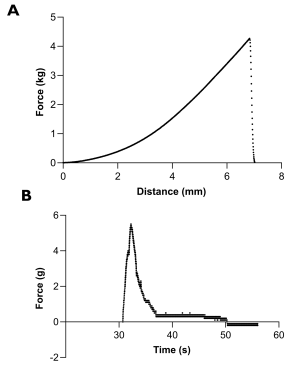

Figure 1. Representation of the material's performance along both tests. **A)** Performance of a sample on the puncture test. **B)** Performance of a sample along the mucoadhesion test.

The functional properties of biomimetic substitutes were similar or superior to those reported in the literature for native TM.

Biocompatibility

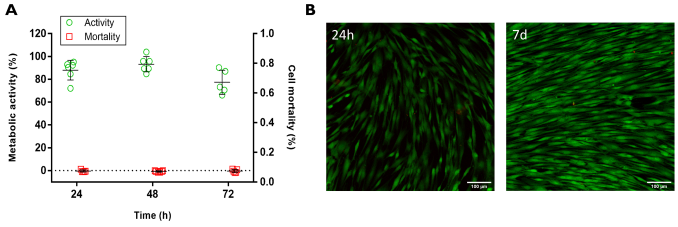

Figure 2. *In vitro* assessment of the biocompatibility of HS27 fibroblast cell line in direct contact with the developed biomaterial. **A)** Cell Counting Kit 8 (green) was used for the evaluation of cell metabolic activity and CellTox Green Cytotoxicity Assay (red) for mortality through 24, 48 and 72 hours of cell culture. **B)** LIVE/DEAD™ Viability/Cytotoxicity Kit was employed along a week in order to assess the cell viability (green) and mortality (red) due to exposure to the scaffold.

The scaffolds were fully biocompatible with no relevant affection of cell viability over the one-week period.

WHAT'S NEXT?

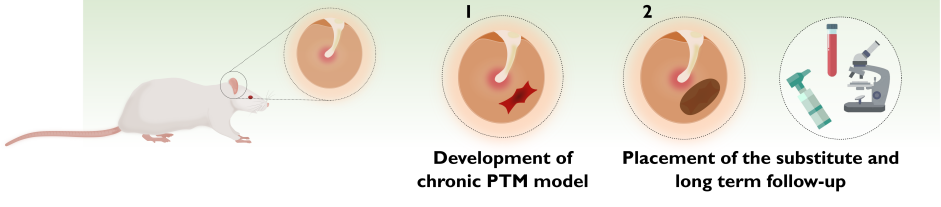

Figure 3. Representation of the workflow for the evaluation of the regenerative capacity of TM substitutes in rat PTM models.

ACKNOWLEDGEMENTS

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