

An advanced strategy for the treatment of chronic wounds: rhEGF loaded nanostructured lipid carriers (rhEGF-NLC) enhance the healing of full-thickness excisional wounds in *db/db* mice

Garazi Gainza¹, Marta Pastor¹, Silvia Villullas¹, Jose Javier Aguirre^{1,4}, Francisco Borja Gutierrez⁴, Enara Herran¹, Oihane Ibarrola¹, Angel del Pozo¹, Jose Luis Pedraz^{2,3}, Rosa M^a Hernandez^{2,3}, Manoli Igartua^{2,3}, Eusebio Gainza¹

¹BioPraxis AIE, Hermanos Lumière 5, 01510 Miñano, Spain

²NanoBioCel Group, Laboratory of Pharmaceutics, School of Pharmacy, University of the Basque Country (UPV/EHU), Vitoria, 01006, Spain

³Biomedical Research Networking Center in Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN), Vitoria, 01006, Spain

⁴Anatomic Pathology Service. Hospital Universitario de Álava (HUA) Txagorritxu, Vitoria, 01009, Spain
ggainza@praxisph.com

Abstract

INTRODUCTION

Chronic wounds represent a major clinical challenge for the health care systems due to their increasing incidence. Currently, the risk of suffering from chronic wounds has increased alarmingly, resulting in about the 2 % of the total European Health budgets [1]. Therefore, the development of advanced drug delivery systems (DDS) to improve the effectiveness of the current treatments and, thus, the quality of life of the patients, has become a major need. In the current work rhEGF loaded nanostructured lipid carriers (rhEGF-NLC) were prepared and their efficacy was tested *in vitro* in BALB/c fibroblast and after topical administration in a full-thickness excisional wound model in *db/db* mice.

RESULTS AND DISCUSSION

rhEGF-NLC were prepared by a simple melted emulsification method. Remarkably, the *in vitro* proliferation studies evidenced that the rhEGF-NLC bioactivity was even higher than free rhEGF, suggesting that the nanoencapsulation process may promote the affinity of the rhEGF to the EGF receptor and, this could strongly impact on the cell proliferation rate.

The *in vivo* studies revealed that 2 topical administrations of 10 or 20 µg rhEGF-NLC not only reduced the wound area by day 8 more than the control groups (untreated and empty NLC controls), but also improved the wound closure compared with 2 intralesional doses of 75 µg of free rhEGF (Figure 1A). In addition, the histological examination of the wound maturation and healing quality revealed that the lesions treated with topically administered rhEGF-NLC, regardless the dose, showed an improved healing quality than controls and a similar efficiency than a greater dose of free rhEGF administered by intralesional infiltrations (Figure 1B). Finally, the study of the re-epithelisation grade revealed that the groups treated with 20 µg rhEGF-NLC improved the re-epithelisation compared with 2 doses of 75 µg free rhEGF, however, significant differences were not achieved among the lesions treated with 10 µg rhEGF-NLC and controls. Overall, we demonstrate the promising effect of rhEGF-NLC to promote faster and more effective wound healing, and suggest its possible application in chronic wounds treatment.

References

[1] Mustoe, TA. et al. (2006). Chronic wound pathogenesis and current treatment strategies: a unifying hypothesis. *Plast Reconstr Surg.* (7 Suppl):35S-41S.

Figures

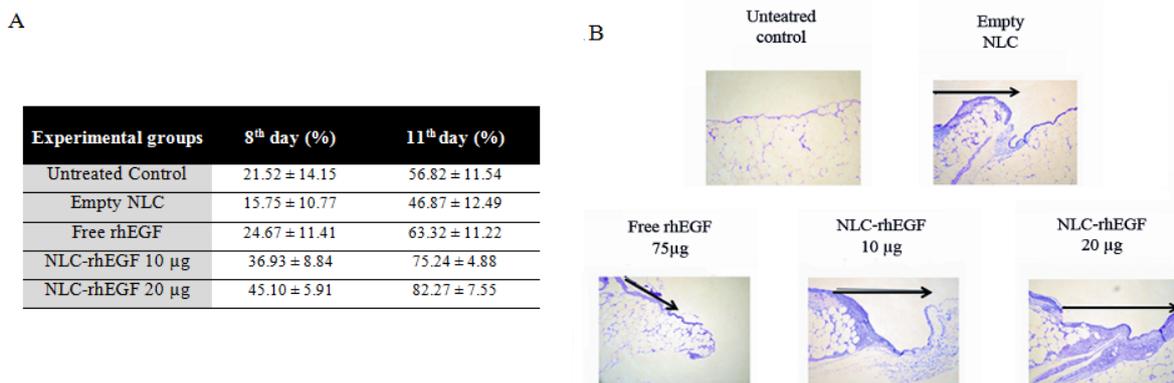


Figure 1. Results obtained from the *in vivo* studies. (A) Wound closure percentages on day 8 and 11 after the wound creation. (B) Histological images of the wounds by day 8; the slides were stained with H&E.