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Lactobacillus rhamnosus GG Increases the Re-Epithelialization Rate of Model Wounds by Stimulating Keratinocyte Migration in Ex-Vivo

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Abstract : Many studies have demonstrated the importance of probiotics and their potential therapeutic effects within the gut. Recently, the possible therapeutic effects of probiotics in other tissues have also begun to be investigated. Comparatively few studies have evaluated the use of topical probiotics in relation to the skin. In this study, we have conducted preliminary investigations into whether a well-known probiotic, Lactobacillus rhamnosus GG (LGG), can increase the rate of re-epithelialization in a model wound. Full-thickness skin was obtained from individuals undergoing elective cosmetic surgery. This skin was wounded using excisional punch and cultured using a serum-free medium, either in the presence or absence of L. rhamnosus GG lysate. Histological staining of the sections was performed with Haematoxylin& Eosin E to quantify "epithelial tongue length". This is the length of the new epithelial 'tongue' that grows and covers the exposed dermis at the inner wound edges. The length of the new epithelial 'tongue' was compared in untreated section and section treated with and L. rhamnosus GG made using108CFU/ml bacterial cells. L. rhamnosus GG lysate enhanced significantly the re-epithelialisation of treated wounds compared with that of untreated wounds (P=0.005, n=3). Tongue length, at day 1 was 7.55μm 0.15, at day 3 it was 18.5μm 0.25 and at day 7 was 22.9μm 0.35. These results can be compared with untreated cultures in which tongue length was 3.25μm 0.35, day 3 was 9.65μm 0.25 and day 7 was 13.5μm 0.15 post-wounding. In ex-vivo proliferation and migration cells were measured by determining the expression of nuclear proliferation marker Ki-67 and the expression of Phosphorylated cortactin respectively demonstrated that L. rhamnosus GG significantly increased NHEK proliferation and migration rates relative to controls. However, the dominant mechanism was migration because in ex-vivo skin treated with the L. rhamnosus GG up-regulated the gene expression of the chemokine receptor and ligands CXCR2 and CXCL2 comparing with controls (P=0.02, P=0.03 respectively, n=3). High levels of CXCL2/CXCL2 have already been implicated in multiple aspects of stimulation of wound healing through activation of keratinocyte migration. These data demonstrate that lysates from Lactobacillus rhamnosus GG increase re-epithelialization by stimulation of keratinocyte migration. The current study identifies the partial mechanism that contribute to stimulating the wound-healing process ex vivo in response to L. rhamnosus GG lysate is an increase in the production of CXCL2/ CXCR2 in ex vivo models. The use of probiotic lysates potentially offers new options to develop treatments that could improve wound healing.

Keywords : Lactobacillus rhamnosus GG, wounds, migration, lysate
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