Academy of Romanian Scientists *Volume 10, No. 2, 2021, pp. 7-21*
Annals Series on Biological Sciences Online ISSN 2285 – 417

ORIGINAL PAPERS

Efficacy of Chitin and Keratin Bioactive Fractions in Skin Inflammatory Processes Remission

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Abstract. The development of new therapies in the field of regenerative medicine is a priority area, which integrates, among other fields of research, the use of active molecules from extracts of natural origin with renewable potential. In this context, the biomedical applications of chitin from various natural sources (entomological, marine etc.), as well as those of keratin from leather waste, are included. The studies we initiated show the effectiveness of the Valke fraction of keratin, isolated from sheep's wool, and that of type L (from insects) and R (from crustaceans) chitin preparations, in modulating cellular processes specific to skin tissue degradation: IL6, IL8, IL1α cytokine-directed inflammation, angiogenic repairing processes (extracellular VEGF) and oxidative stress (oxygenated free radicals). The cellular response of keratinocytes from a HaCaT line under induced inflammation (LPS and TNFα) is manifested by increased intracellular levels of oxygenated free radicals, counteracted mainly by chitin. In case of bacterial infections simulated in vitro with LPS polysaccharide, the anti-inflammatory effects induced by Valke keratin on IL6-directed signaling pathways (acute phase cytokine behavior) are noticeable. Moreover, the same effects are reflected through the inhibition of IL8, the chemokine responsible for neutrophil recruitment to the inflammatory site. Nonetheless,

chitin reduces the release of IL6, while strongly stimulating VEGF for "de novo" angiogenesis in the injured tissue. In addition, the pro-irritant cytokine IL1α is inhibited by chitin and keratin, which suggests a reduction in the epidermal irritant potential. The results guide the applications to several etiologies wound therapy. The studies were carried out within 5 PTE Project / 2020 – BIOTEHKER.

Keywords: *keratin, chitin, keratinocytes, TNFα, LPS*

DOI https://doi.org/10.56082/annalsarscibio.2021.2.7

1. Introduction

The development of new therapies in the field of regenerative medicine is a priority area, which integrates, among other fields of research, the use of active molecules from extracts of natural origin with renewable potential, in order to develop a sustainable bioeconomy, with the full exploitation and conservation of biological resources. In this context are included the biomedical applications of chitin from various natural sources (entomological, marine, etc.), as well as those of keratin from leather waste (e.g. sheep wool).

Due to its size, characteristics and roles, human skin has been the most intensly tested organ for its regenerative capabilities and it has shown promising results. The impact of effective skin tissue regeneration is major, because the skin is affected in the most diverse pathologies, trauma and infections, being our first and main defense organ in the face of the external environment.

Thus, correct and rapid regeneration of the skin can change the trajectory of the disease and the general condition of the patient in the following conditions: bedsores, flame / solar burns, diabetes mellitus, cuts, hemorrhoids, post-operative recovery, extremely diverse dermatological diseases: from dermatitis, to psoriasis and up to epidermolysis bullosa. Rapid regeneration of the skin, assisted through conditions as similar as possible to the physiophysical ones, leads to an increased impliance and an accelerated recovery of the patient, decreasing their vulnerability time to other complications associated with the difficult healing of a wound (risk of infection, depression, aggravation of the wound, amputation, immobility etc.). The regulation of wound healing is critical because inappropriate proinflammatory signaling can result in wounds that heal harder and are at risk of infection [1,2]. Non-healing wounds usually cause distress and require careful management [1]. If the switch to proliferative signaling is not carefully controlled, then repair can result in fibrosis, which implies excessive accumulation of ECM proteins, such as collagen, at the site of injury/damage. Scar formation is the normal end point of mammalian tissue repair, however, excessive scarring can impair normal tissue function [1,3]. Fibrotic skin tissue’s spectrum of severity ranges from flat, pale and relatively static atrophic scars to severe, highly pigmented, rapidly growing, pathological, hypertrophic and keloid scars. Even the