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Basic research

Healing efficiency of oligosaccharides generated from almond gum (*Prunus amygdalus*) on dermal wounds of adult rats

Fatma Bouaziz [a], Molka Ben Romdhane [a], Claire Boisset Helbert [b], Laurine Buon [b], Fatma Bhiri [a], Sana Bardaa [c], Dorra Driss [a], Mohamed Koubaa [a], Akram Fakhfakh [a], Zouhair Sahnoun [c], Fatma Kallel [a], Najiba Zghal [d], Semia Ellouz Chaabouni [a,e,*]

[a] *Enzyme Bioconversion Unit (04/UR/09-04), National School of Engineering, P.O. Box 1173-3038, Sfax University, Tunisia*
[b] *Centre de Recherches sur les Macromolécules Végétales, C.N.R.S., Université Joseph Fourier, BP 53, Grenoble Cedex 9 38041, France*
[c] *Pharmacology Laboratory (UR 15/04), Sfax Medicine Faculty, 3029, Sfax University, Tunisia*
[d] *Animal Physiology Laboratory (UR 11/ES-70), Sfax Science Faculty, P.O. Box 1171-3000, Sfax University, Tunisia*
[e] *Common Service Unit of Bioreactor Coupled with an Ultrafilter, National School of Engineering, P.O. Box 1173-3038, Sfax University, Tunisia*

KEYWORDS
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Abstract Almond gum is a naturally occurring polymer produced by almond trees and shrubs. Its abundance, as well as its low cost production makes it a potential feedstock for use in food and pharmaceuticals. In this regard, almond gum oligosaccharides were enzymatically generated, purified and their monosaccharide composition assessed using gas chromatography-flame ionization detector. Oligosaccharide analyses show that the most prominent residues were galactose and arabinose with traces of xylose, rhamnose, glucose and mannose. The glycosyl linkage positions were analyzed using gas chromatography — mass spectrometry

Abbreviations: OAG, oligosaccharide almond gum derivatives; *COAG*, cream formulation supplemented with *OAG*.

* Corresponding author. Common Service Unit of Bioreactor Coupled with an Ultrafilter, National School of Engineering, P.O. Box 1173-3038, Sfax University, Tunisia. Tel.: +216 74 67 53 31; fax: +216 74 27 55 95.
E-mail address: semia.chaabouni@enis.rnu.tn (S. Ellouz Chaabouni).

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showing a main chain composed of galactose units [→3)-Gal-(1→] branched mainly with arabinose residues [Ara-(1→]. The potent role of the generated oligosaccharides on rats wound healing was investigated. They have been applied either alone or supplemented, as active substance, with cream formulation, on full-thickness wound created on the dorsum of the rats. The effect of oligosaccharides was assessed by measuring the wound closure percentage, reaching an average of around 100% when applied alone or supplemented to cream formulation. The healing percentage for the control group was only 74.3% at the same day. The histological evaluation of skin sections visualized by light microscopy revealed an improved collagen deposition and an increased fibroblast and vascular densities.

Introduction

Wounds are physical injuries that result in an opening or break of the skin. Healing is a complex and intricate process initiated in response to an injury that restores the function and integrity of damaged tissues. Wound healing involves continuous cell—cell and cell—matrix interactions that allow the process in three overlapping phases; inflammation (0—3 days), cellular proliferation (3—12 days) and remodeling (3—6 months) [1]. In fact, platelet aggregation during hemostasis releases a number of soluble mediators starting the healing process [2]. Hemostasis is followed by an early inflammatory phase characterized by vasodilatation, increased capillary permeability, complement activation and polymorphonuclear and macrophage migration into the wound within three days [3].

The availability of drugs able to stimulate the process of wound healing is still limited. Only 1—3% of the drugs listed in western pharmacopoeias are intended to be used on wounds [4]. The use of natural molecules and polymers, as remedies or for tissue engineering, is actually a major approach to repair and/or regenerate tissues [5,6].

Recently, interesting stimulating effects on human skin cell physiology have been shown using plant polysaccharides [7—10]. The strong enhancement of cell viability and proliferation rates in human skin fibroblasts and keratinocytes suggests a positive impact of some carbohydrates on skin regeneration [11]. In fact, it has been reported in previous studies that chitin and chitosan polysaccharides induced the activation of a complement system [12], polymorphonuclear cells [13], fibroblasts and vascular endothelial cells [14]. Additionally, heparin polysaccharides are currently used for the treatment of skin and eye ulcers [15]. Moreover, a family of dextran derivatives and glycosaminoglycans are well known for their comforted therapeutic potential [16,17]. However, regarding the critical uses of these complex polymers in clinical applications due to their structure complexity, the therapeutic fields gave increasing importance to oligosaccharides to replace polymeric structures [18]. In fact, it has been shown that chitosan oligosaccharides could be used as wound dressings [19] and may suppress LPS-induced IL-8 expression in human umbilical vein endothelial cells [20]. Moreover, oligosaccharides of hyaluronic acid increased epidermal cell stemness [21] and promote excisional wound healing through enhanced angiogenesis [22]. It has been reported previously that oligosaccharides generated by enzymatic or chemical hydrolysis of exudate gums, exhibit potent biological activities such as acarbose acting as antidiabetes [23—25], glucose oligomers acting as anticancer drugs [26], and sucralfate acting for epithelial wound healing [27,28].

Despite the huge availability of almond gum in the mediterranean countries (*e.g.* Tunisia), its application on dermatology remains widely ignored. The aim of this work was first, to isolate, purify and characterize oligosaccharides from almond gum (*OAG*), then to investigate their capacity on wound healing, using rats as model. To the best of our knowledge, this work is the first, highlighting the potential role of *OAG* as an agricultural by-product on dermal wound healing.

Materials and methods

Products and chemicals

Almond gum was collected from almond trunks (Achaak variety) in the suburb of Sfax city in Tunisia. Zinc acetate and potassium ferrocyanure were purchased from LOBA Chemie (Mumbai, India). Commercial cream; CICAFLORA®, used as reference, was provided by "Labo MHF" (Mohamed