

Oligosaccharidic fractions derived from *Triticum vulgare* extract accelerate tissutal repairing processes in in vitro and in vivo models of skin lesions

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Abstract

Ethnopharmacological relevance

Triticum vulgare has been extensively used in traditional medicine thanks to its properties of accelerating tissue repair. The aqueous extract of *Triticum vulgare* (TVE) is currently an active component used by Farmaceutici Damor in the manufacture of certain pharmaceutical products already marketed in Italy and abroad under the brand name Fitostimoline[®], in the formulation of cream and medicated gauze and is commonly used for the treatment of decubitus ulcers, sores, burns, scarring delays, dystrophic diseases, and, more broadly, in the presence of problems relating to re-epithelialization or tissue regeneration. The active components of Fitostimoline[®]-based products determine a marked acceleration of tissutal repairing processes, stimulate chemotaxis and the fibroblastic maturation, and significantly increase the fibroblastic index, which are crucial points in the repairing processes. The aim of the present paper was to identify and characterize the active fractions of TVE responsible for the pharmacological effect in tissutal repairing processes.

Materials and methods

Several fractions obtained from TVE by ultrafiltration procedures and HPAE chromatography were tested to measure their growth-enhancing activity on NIH-3T3 fibroblasts. The healing action of the same fractions, prepared as cream formulation, was assessed in rat subjected to two different models of skin lesion, skin scarification and excision.

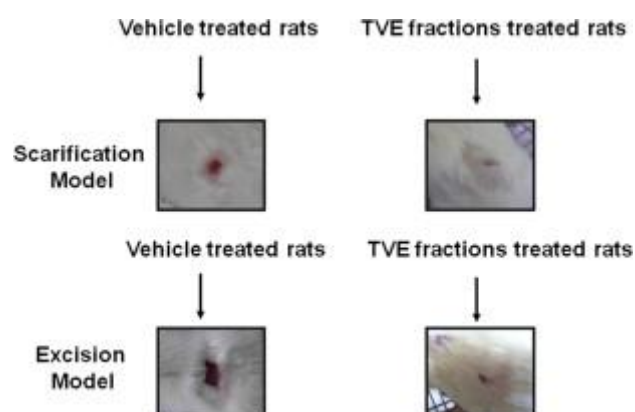
Results

Our results showed a pro-proliferative effect of the fractions ST-98 and K>1000 in NIH-3T3 fibroblasts. Moreover these fractions formulated as cream preparations were effective also in in vivo models of skin lesion.

Conclusions

The results of the present study showed that these active fractions of TVE are responsible for its pro-proliferative effect.

Graphical abstract



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Introduction

In recent years one of the main aims of biological and clinical research has been the isolation and identification of factors which facilitate and enhance normal wound healing processes in animals and humans. The presence in mammalian cells of specific factors responsible for accelerating the healing process (Ten Dijke and Iwata, 1989) and the existence of compounds within plants such as *Centella asiatica* and *Gardenia jasminoides* Ellis fructus (Morisset et al., 1987), still only partially identified, with these pharmacological properties have been well established. The aqueous extract of *Triticum vulgare* (TVE) obtained from the whole germinated plant and containing mainly oligosaccharidic components has different biological properties including a mitogenic effect both in plants and in the mouse fibroblast line BALB/c NIH-3T3 (Farinella et al., 1986, Favit et al., 1992), useful in the process of wound healing.

Moreover the aqueous extract of *Triticum vulgare* is currently an active component used by Farmaceutici Damor in the manufacture of certain pharmaceutical products already marketed in Italy and abroad under the brand name Fitostimoline®, in the formulation of cream and medicated gauzes and is commonly used for the treatment of decubitus ulcers, sores, burns, scarring delays, dystrophic diseases, and, more broadly, in the presence of problems relating to re-epithelialization or tissue regeneration (Chaturvedi et al., 2010, Martini et al., 2011, Serafini and Saponati, 2012).

Triticum vulgare has been extensively used in traditional medicine thanks to its properties of accelerating tissue repair. In particular, scientific evidence documented that the wheat sprout oil has been used in traditional Iranian medicine for dermatonic and skin beauty, face freckles, moisturizing and repair the minute pores of the face skin (Mikaili et al., 2012).

The active components of Fitostimoline®-based products determine an acceleration of tissutal repairing processes, stimulate chemotaxis and the fibroblastic maturation, and significantly increase the

fibroblastic index, which are crucial points in the repairing processes (Viano and Santiano, 1978, Fiore et al., 1993). It has been suggested that these activities are due to the accelerated protein synthesis and to the enhanced ability of captation and incorporation of marked proline from tissues (Viano and Santiano, 1978, Fiore et al., 1993, Vanden Berghe et al., 1993).

With the aim of identifying and characterizing the active fractions of TVE responsible for its pharmacological effect, in the present study we investigated the effect of several fractions obtained from TVE on the growth of mouse fibroblast NIH-3T3 cells, that have been chosen as an appropriate in vitro experimental model for our studies since TVE has been shown to enhance the growth of mouse fibroblast NIH-3T3 cells (Farinella et al., 1986). For this purpose the fractions have been isolated by ultrafiltration procedures and HPAE chromatography and their growth-enhancing activity on NIH-3T3 fibroblasts has been determined and compared with those of the crude TVE and fetal bovine serum (FBS). Here we report that the effect of some fractions on the growth of mouse fibroblast NIH-3T3 cells assessed by proliferation assays and scratch tests is comparable to that of the whole aqueous extract of *Triticum vulgare*.

Furthermore, we have investigated the healing action of these in vitro active fractions in two different in vivo models of skin lesion, skin scarification and excision in rats. The healing action was evaluated 3 or 7 days after skin damage induction.

Section snippets

Plant description

Triticum vulgare, the binomial scientific name of a plant of Gramineae family, is the commonly known wheat plant. It is grown under controlled conditions in the laboratory of Farmaceutici Damor, Naples, Italy. The voucher specimen is DF/237/2014 and is deposited in the herbarium of the Medical Botany Chain of University of Salerno, Italy. The commercially available seeds are purchased from Consorzio Agrario Lombardo Veneto from Northern Italy. The batch number for the seeds used for the

Preparation and chromatographic profiles of tested fractions

Two batches of *Triticum vulgare* extract (TVE K0801 and K0901) were prepared according to standard manufacturing protocol at Farmaceutici Damor. Successively, to obtain 2 whole fractions with different molecular weights, 1 L of TVE K0901 was submitted to molecular weight fractionation through a standard ultrafiltration procedure in an Amicon 200 ml ultrafiltration cell equipped with a Millipore NMWL 1000 Da membrane of 63.5 mm (2 bar N₂ pressure). The concentrated fraction (labeled K>1000),

Discussion and conclusions

The present paper describes a pro-proliferative effect of the fractions ST-98 and K>1000 of TVE in in vitro and in vivo models of skin lesion; thus indicating the active fractions of TVE responsible for its pro-proliferative effect.

The aqueous extract of *Triticum vulgare* possesses a number of biological properties including a mitogenic effect both in plants and in the mouse fibroblast line BALB/c NIH-3T3 (Farinella et al., 1986, Favit et al., 1992), indicating potential properties of this

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