United States Patent **4,760,131**
***Sundsmo* , et al.** **July 26, 1988**

Wound-healing composition

Abstract

A soft tissue ***wound*** healing composition comprising an aqueous mixture of fibrillar collagen, heparin, and undegranulated platelets or platelet releasate. The composition is applied topically to the ***wound*** site in conjunction with means to keep it at the site and hydrated or in the form of an occlusive dressing.

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Parent Case Text

CROSS-REFERENCE TO RELATED APPLICATION
This application is a continuation-in-part of copending application Ser. No. 855,508, filed Apr. 23, 1986 and now abandoned.

Claims

We claim:

1. A soft tissue ***wound*** healing composition comprising an aqueous mixture of:
(a) fibrillar collagen at a concentration in the range of about 1 to about 70 mg/ml;
(b) about 0.1% to about 10% by weight based on collagen of a glycosaminoglycan selected from the group consisting of heparin, a heparin-like glycosaminoglycan, and mixtures thereof; and

(c) about 0.01% to about 10% by volume based on collagen of undegranulated platelets or an equivalent amount of platelet releasate.

MODES OF CARRYING OUT THE INVENTION

The composition of the invention is useful for treating soft tissue wounds such as cutaneous, dermal, mucosal or epithelial wounds in vertebrates. It is especially useful for treating cutaneous wounds in mammals including man, domestic and farm animals, sports animals, and pets. It may be used to treat any type of full or partial thickness cutaneous wounds including traumatic wounds, surgical wounds, thermal or chemical wounds (burns), radiation wounds and chronic ulcers such as decubiti, and cutaneous ulcers caused by vascular, hematologic and metabolic diseases, infections, or neoplasms.

The collagen that is used in the invention is fibrillar and is capable of binding heparin or heparin-like glycosaminoglycans. Type I or Type III collagen, or mixtures thereof, are preferred because of their heparin binding capacity. The collagen may be of genetically dissimilar origin (e.g., allogeneic or xenogeneic) than the individual to which it is applied. If the collagen is xenogeneic it is preferred that it be purified to lessen or reduce the likelihood of immunogenicity. The collagen fibers may be native or reconstituted and may be cross-linked or uncross-linked. Bovine dermal fibrillar collagen suitable for use in the composition is available commercially under the trademark ZYDERM.RTM. from the assignee of this application. The fibrillar collagen is in the form of an aqueous suspension or gel in which the concentration of collagen is in the range of about 1 to 70 mg/ml. A collagen concentration range of 15 to 35 mg/ml is preferred for handling purposes. Depending upon the concentration of collagen the consistency of the final mixture will range from a translucent gel to a runny syrup.

Heparin or a heparin-like glycosaminoglycan is mixed with the fibrillar collagen in amounts ranging between about 0.1% to about 10% by weight, based on collagen, preferably about 0.3% to 3%, and most preferably about 1%. Heparin is a staple product of commerce. Fragments and derivatives of heparin are known which possess chemical similarity to heparin. As used herein the term "heparin-like glycosaminoglycan" is intended to include such fragments and derivatives, provided they are functionally equivalent to heparin in the composition (i.e., combine with collagen and platelets to provide efficacious ***wound*** healing).

The platelets that are used in the invention are isolated from vertebrate blood, preferably mammalian blood, under conditions which prevent degranulation. Such conditions are well known and typically involve mixing the blood with an anticoagulant solution and centrifuging the platelets from the mixture. The mammalian species of the platelets are diluted in buffer and then added to the fibrillar collagen-heparin mixture. The final volume dilution of platelets, expressed in terms of volume of packed platelets, is in the range of about 1:10 to 1:10,000, preferably 1:50 to 1:100. Expressed in terms of volume % based on collagen, the packed platelets are added to the mixture at levels in the range of 0.01% to 10%, preferably 2% to 10%.

Platelet releasate may be used as an alternative to whole platelets. The releasate comprises granule constituents that are released after aggregation and that possess angiogenic activity, chemotactic activity, mitogenic activity, connective tissue deposition activity, or epidermal cell proliferation activity. It may be prepared by sonicating platelets or treating a platelet suspension with agents that cause the platelets to aggregate and release granule constituents. Examples of such agents are thrombin, collagen, ADP and immune complexes. After such treatment solids (e.g., cellular debris, aggregated platelets) are separated, such as by centrifugation. The releasate may be purified by affinity chromatography using a heparin-Sepharose column. The amount of releasate used in the mixture is that which is equivalent to 0.01% to 10% by volume, preferably 2% to 10%, based on collagen of packed platelets. In other words, one uses that amount of releasate that is derived from such an amount of packed platelets.