

## COMPOSITION AND PROCESS FOR PROMOTING EPITHELIAL REGENERATION

This is a continuation-in-part of application Ser. No. 619,004, filed June 11, 1984 for Treatment of Epithelial and Connective Tissue and Composition Therefor, which was a continuation-in-part of application Ser. No. 341,544, filed Jan. 21, 1982 for Treatment of Vaginitis and Cervicitis, both now abandoned.

The present invention relates to a composition for treating the surface epithelium and to a process for promoting epithelial regeneration.

Epithelial tissue covers the entire body, including the internal surfaces of the gastrointestinal tract, genitourinary tract, respiratory tract and reproductive tract and serves to protect the body against injury. When the epithelium is injured, it is well known that the process of healing is complex and begins with cell migration, division, differentiation and production of special products. In some cases, granulation tissue is formed to fill the gap between the edges of the wound with a thin layer of fibrinous exudate consisting of epithelial cells, fibroblasts, endothelial cells, blood-borne cells (e.g., macrophages, lymphocytes, neutrophils and platelets), collagen and glycosaminoglycans. The process of wound healing includes homeostasis (i.e., processes through which bodily equilibrium is maintained), angiogenesis (i.e. production of blood vessels) and fibroplasia (i.e. production of fibrous tissue). The key to understanding the healing process resides in the interaction among the forces of healing, coagulation and inflammation. When the result of healing closely approximates the normal state the process is referred to as regeneration.

When the epithelium is injured, the amount of zinc, vitamin C, cystine and many other nutrients is reduced in the affected cells. Up until the present time, however, it was not known that the topical application of a combination of zinc salt, vitamin C and sulfur amino acid would be particularly effective at promoting epithelial regeneration.

In view of the above, it is an object of the present invention to provide a composition which promotes epithelial regeneration with a unique combination of materials which, in its preferred form, are present in epithelial tissue at very low levels. Other objects and features will be in part apparent and in part pointed out hereinafter. The invention accordingly comprises the compositions and methods hereinafter described, the scope of the invention being indicated by the subjoined claims.

In accordance with the present invention, a mixture of zinc salt, vitamin C and sulfur amino acid is formed for addition to a pharmaceutical carrier. For use herein, the zinc is provided in a salt form wherein the anion is non-toxic to the subject such as sulfate. The vitamin C may be provided as ascorbic acid, sodium ascorbate or the like and cystine may be replaced with other sulfur amino acids which inhibit collagenase and in general is selected from the group consisting of cystine, cysteine, methionine and di- and tripeptides such as glutathione formed therefrom. A mucopolysaccharide may be included for some applications. Suitable mucopolysaccharides are extracted from animal or plant connective tissue with different mucopolysaccharides being preferred depending on the nature of the epithelium being treated. For example chondroitin sulfate and hyalu-

ronic acid are preferred in the reproductive tract, heparin calcium salt, dermatan sulfate or mucopolysaccharides extracted from aloe vera plant are preferred for skin ulcerations and keratan sulfate is preferred for treatment of the eyes.

A polysaccharide may also be included in the formulation if the surface to be treated is slippery. Suitable polysaccharides include agar, algin, carboxymethylcellulose, carrageenan, guar gum, gum arabic, gum ghatti, gum tragacanth, hydroxyethylcellulose, hydroxypropylguar, karaya gum, locust bean gum, methylcellulose, pectin and xanthan gum.

In accordance with the present invention, the zinc is present in an amount from about 0.25 to 20% by weight as zinc sulfate heptahydrate or the equivalent amount of zinc present as some other zinc salt. As shown in the examples, the preferred amount of zinc depends on the condition being treated. For example, when the medication is a douche for treating vaginitis or cervicitis and the subject is a menstruating female, the zinc is preferably present in an amount from about 1 to 2% by weight but when the subject is pre- or postmenopausal, less zinc is required with the preferred amount being from about 0.25 to 0.5% by weight.

The vitamin C is present in an amount from about 0.5 to 30% by weight, preferably from about 3 to 10% and most preferably from about 5 to 10%. The cystine or other sulfur amino acid is present in an amount from about 0.25 to 5% by weight, preferably from about 0.25 to 1% and most preferably from about 0.25 to 0.5%. The mucopolysaccharide, when present, is present in an amount from about 0.05 to 10% by weight, preferably from about 0.05 to 2% and most preferably from about 0.05 to 0.5%.

The medication can be used to treat a wide variety of conditions. For example, in the reproductive tract it can be used to treat vaginitis and cervicitis. In the genitourinary tract, it can be used to treat urethral infections, especially the irritated bladder of schistosomiasis patients, and in the eyes it can be used to treat extropian eyelids, blepharitis, keratitis, and pinkeye and to prevent cataracts and diabetic retinopathy. On the skin, it can be used to treat burns, cuts, fever blisters, poison ivy, chigger bites, diaper rash, genital herpes blisters and even sunburn. The conditions listed above indicate the scope of the invention and are not meant to be limiting. Depending on the locus of the treatment and the method of application, the medication can be formulated in an appropriate water, oil or gel vehicle; spray, powder or medicated bandage, for example.

The following examples illustrate the invention.

### EXAMPLE 1

Eighty Charles River variety white male rats, weighing about 150 g were divided randomly into 8 groups of 10 animals each, 2 control and 6 treatment groups:

C1—Control/burn only (After treatment these animals were kept out of the infectious area)

C2—Control/burn

T1—Burn/Ointment containing 2% ascorbic acid

T2—Burn/Ointment containing 2% zinc sulfate

T3—Burn/Ointment containing 2% cysteine

T4—Burn/Ointment containing 2% ascorbic acid and 2% zinc sulfate

T5—Burn/Ointment containing 2% ascorbic acid and 2% cysteine

T6—Burn/Ointment containing 2% ascorbic acid, 2% zinc sulfate and 2% cysteine.