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(54) Title: ANTIMICROBIAL COMPOSITION

(57) Abstract: A complex antimicrobial sorption composition possessing the necrolytic effect for treating the purulent wounds, the trophic ulcers, the wounds, and the infiltrates with the significant necrotic and exudative components represents the silica sorbent with the immobilized drug. Aerosil is used as a siliceous sorbent, and seratiopeptidase as a drug.

ANTIMICROBIAL COMPOSITION

Field of the Invention

The invention concerns new substances based upon fine pyrogenic silica, or aerosil (commercial pharmaceutical names Silard P, Silex, Atoxil) that contains serrathiopeptidase immobilized thereon. Such composition is active in the lyzis of necrotizing tissues, cleanses wound surfaces, improves blood supply to tissues, eliminates an objectionable putrificient odour, has an anti-edematous effect.

Background of the Invention

Treatment of festering wounds with an apparent necrosis of tissues, especially where significant exudation is evident, presents a very complicated problem, since there are very few therapeutic compositions available to cope with the processes [1, 2].

Conventional preparations that are used in the course of contaminated surgery and have quite a good antibacterial effect are not sufficiently effective in inhibiting necrosis. Where the preparations are indeed effective, they have an ointment form, feature a low sorptive capacity and would not be easily removed when dressings are replaced (ophlotrimol-P, iruxol) [3].

Moreover, they all have no antihypoxic effect, are nondurable, and therefore do not produce any stable effect in the treatment of suppurative complications in soft tissues, which complications result in considerable necrosis.

The preparation bearing closely on the invention is known as "Imosgent" and comprising a xerogel of methylsilicic acid with the antibiotic gentamicin immobilized thereon [4]. This preparation has a durable antimicrobic effect on pathogenic aerobic microorganisms and is effective for the treatment of burns and festering wounds. Yet this preparation is insufficiently effective in the treatment of suppurative complications in soft tissues, which complications result in necrosis of the tissues, it does not improve blood supply to the tissues, has no antihypoxic and sorptive action.

Summary of the Invention

According to the invention there is provided an antimicrobial composition substantially consisting of a siliceous sorbent and a medicinal agent immobilized thereon, wherein the siliceous sorbent is pyrogenic silica and the medicinal agent is serrathiopeptidase, both present in the following amounts, % by weight:

pyrogenic silica	99 to 90
serrathiopeptidase	1 to 10.

This invention contemplates the antimicrobial composition for use as a medicament for the treatment of festering wounds, trophic ulcers and burns, infiltrations with marked necrotic and exudative components.

The invention also consists in the provision of a method for treating festering wounds, trophic ulcers and burns, infiltrations with marked necrotic and exudative components by applying the antimicrobial composition of the present invention topically to the surface of a wound.

Best Mode for Carrying Out the Invention

Such a composition was not known before.

Aerosil is fine pyrogenic silica, that consists of hydrated globules of an average radius of 4.35 nm, aerogel of polisilicic acid $SiO_2 \cdot x\ H_2O$, the water content being up to 10% by weight. Aerosil may be used orally as enterosorbent and as a matrix for immobilizing medical products.

The composition of the invention hereinafter referred to as Sertasil is obtained in the following way.

The method of obtaining Sertasil.

The method of obtaining consists in the formation of a solution or a suspension of serrathiopeptidase in a proper solvent in a predetermined proportion, that is added to a solid adsorbent (aerosil, polimethylsiloxane and so on) by means of impregnation, and subsequent lyophilic, vacuum or air drying at temperatures below 40-45°C until obtaining a light air-dry white powder or as a result of mechanical dispersion of an active substance on the adsorbent surface.

Examples of preparing Sertasil are set forth below.

Example 1.

100 mg of serrathiopeptidase are dissolved in 100 ml of distilled water and stirred for 30 to 60 minutes at room temperature. Then Aerosil A-300 in the amount of 10 g is added into the solution while the stirring is continued. The mixture thus obtained is dried in vacuum at a temperature of 30°C. A granular white powder is formed.

Example 2.

16 mg of serrathiopeptidase are dissolved in 10 ml of distilled water and stirred for 30 to 60 minutes at room temperature. Then 1 g of Aerosil A-300

(Atoxil) is added into the solution while the stirring is continued. The mixture thus obtained is dried in vacuum at a temperature of 40°C. A granular white powder is formed.

The preparation is used for the treatment of festering wounds, third-degree and forth-degree burns, trophic ulcers of various ethiology where necrosis of the tissues usually occurs. It eliminates odour, removes pus and necrotic tissues from wounds.

It was found that only solutions of serrathiopeptidase containing no more than 0.5% of active substance should be taken for obtaining the preparation Sertasil for use in the treatment of third-degree and forth-degree burns, deep wounds, trophic ulcers with marked necrotic and exudative components.

Septasil was used in the treatment of 47 patients that had deep trophic ulcers, third-degree burns, gangrenes complicated with arteriosclerosis obliterans of low extremities, festering wounds in the exudation stage with marked dense necrosises on their surface, which could not be removed by other methods (including operative intervention), inflammatory infiltrations (resulting from a bullet wound).

Example 1: Patient B., born 1948, was hospitalized with a diagnosis of thermal burns of the right thigh and shank, 4%, III B-degree. The state of the patient was moderate, the body temperature was 38.5°C, the whole surface of the skin and subcutaneous basis in the affected area was necrotized with a dense scab. The operative intervention, namely necrectomy, was performed. Sertasil was applied to the wound surface. After 2 hours the temperature decreased. A complete wound cleansing from necrotic masses took place over 48 hours. Among the preparations of systemic action the patient obtained only anaesthetics and vascular agents (in view of allergic reaction on antibiotics of the most commonly used groups). Henceforth bandages were done with using methyluracilic ointment every 48 hours until complete healing. The wounds healed completely over 17 days.

Example 2: Patient M., born 1964, was admitted to a surgical department with a diagnosis of a bullet wound complicated with inflammatory infiltration of the anterior abdominal wall. On the examination an infiltration 11.0 x 6.5 cm in the left iliac area was found. In the infiltration centre there was a bullet hole 1.5 x 0.7 cm, with a wound channel located from the outside inside, about 3.5 cm

long. Tissues around the wound channel were necrotized, puffed up, dark. At the bottom of the wound channel a bullet was found. The patient on coming in was operated – the bullet was removed, necrectomy was performed. In the postoperative period he took following medicines: cephtriaxon 1.0 g twice daily, intramuscularly, for 5 days, diclofenac sodium 3.0 ml intramuscularly, once daily for 3 days, lidase 64 units once daily, intramuscularly, UHF on the infiltration area during 7 days, daily bandaging with ioddycerin, dioxysole. The performed treatment had no substantional effect: the infiltration kept up previous sizes, no evidence of the wound cleansing and healing was observed. The patient rejected outright the proposed surgical treatment – excising the infiltration. It was decided to cure using the preparation SertaSil by means of administering it in the wound channel after pretreatments with solution of 3% hydrogen peroxide. During next 48 hours the wound channel was completely cleansed from necrotic masses, over 7–8 days since the treatment began, the infiltration became 3.0 x 2.5 cm, the wound channel got superficial, the wound was filled up with granulations and was actively epithelizing. The wound healed over completely and the infiltration resolved over 14 days since the beginning of the treatment with the preparation SertaSil. The patient was inspected in a month – a surface scar about 1.0 x 0.4 cm was found in the area of the former wound and infiltration. The patient made no complaints.

Example 3: Patient K., born 1935, was hospitalized with a diagnosis of chronic venous insufficiency of lower extremities, complicated with trophic ulcer, covered here and there with necrotic tissues. B. Fragilis, E. Coli 10^8 in 1 g of the tissue sample was found on the microbiological examination. After two consecutive dressings with SertaSil, no microbes were detected, the ulcer was completely cleansed in 3 days. Henceforth methyluracilic ointment was used for bandages until the complete healing that occurred in 17 days.

In view of the foregoing, the new preparation Sertasil may be used for local treatment of wounds of various genesis, trophic ulcers, abscesses, infiltrations, burns, etc., with a pronounced necrotic component that cannot be removed by other methods (including an operative one) for various reasons.

Literature.

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The reference in this specification to any prior publication (or information derived from it), or to any matter which is known, is not, and should not be taken as an acknowledgment or admission or any form of suggestion that that prior publication (or information derived from it) or known matter forms part of the common general knowledge in the field of endeavour to which this specification relates.

Throughout this specification and the claims which follow, unless the context requires otherwise, the word "comprise", and variations such as "comprises" and "comprising", will be understood to imply the inclusion of a stated integer or step or group of integers or steps but not the exclusion of any other integer or step or group of integers or steps.

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. An antimicrobial composition substantially consisting of a siliceous sorbent and a medicinal agent immobilized thereon, wherein the siliceous sorbent is pyrogenic silica and the medicinal agent is serrathiopeptidase, both present in the following amounts, % by weight:

pyrogenic silica	99 to 90
serrathiopeptidase	1 to 10.

2. Composition of claim 1 substantially as hereinbefore described with reference to any one of the Examples.

3. Composition of claim 1 or 2 for use as a medicament for the treatment of festering wounds, trophic ulcers and burns, infiltrations with marked necrotic and exudative components.

4. A method for treating festering wounds, trophic ulcers and burns, infiltrations with marked necrotic and exudative components by applying the antimicrobial composition of claim 1 or 2 topically to the surface of a wound.

5. Use of the composition of claim 1 or 2 in the manufacture of a medicament for the treatment of festering wounds, trophic ulcers and burns, infiltrations with marked necrotic and exudative components.