coagulation factor XII is activated due to a stimulation by lesion or invasion of the tissues *in vivo* whereby a series of the enzymatic reactions is induced. Thus, the activated blood coagulation factor XII acts on the plasma prekallikrein existing in the same plasma to convert it to a plasma kallikrein of an activated enzyme type and then the plasma kallikrein acts on the high-molecular-weight kininogen in the plasma to liberate bradykinin.

The bradykinin which is a product of the plasma kallikrein-kinin system exhibits various physiological activities such as dilation of peripheral blood vessels, acceleration of permeation of blood vessels, induction of pain, generation of inflammation, migration of leucocytes, etc. and has been known as a mediator for induction of pain, inflammation and allergic reactions. Accordingly, when an excessive liberation and production of bradykinin is inhibited, it is possible to relieve pain, inflammation, allergic syndromes, etc. and to normalize such disorders.

As mentioned above, bradykinin is liberated and produced in the reaction of the plasma kallikrein with high molecular weight kininogen and, therefore, substances which inhibit the kallikrein production in the plasma kallikrein-kinin system and prevent an excessive production of bradykinin have the possibility of being used as analgesics, antiinflammatory agents, antiallergic drugs, etc. and are highly useful as pharmaceuticals.

According to one aspect of the present invention there is provided a physiologically active substance which is extracted from an activated animal tissue comprising an amorphous and hygroscopic powder containing 1-20 micrograms/mg of at least one silicon component calculated as silicon, the powder being soluble in water, methanol and ethanol and being insoluble in benzene and ether, said powder having a pH of 6.0 to 8.3, and ultraviolet absorptions of λ_{max}=265-275 nm.

According to another aspect of the present invention there is provided a pharmaceutical composition comprising a pharmaceutically effective amount of physiologically active substance which is extracted from an activated animal tissue, said substance comprising an amorphous and hygroscopic powder containing 1-20 micrograms/mg of at least one silicon component calculcated as silicon, the powder being soluble in water, methanol and ethanol and being insoluble in benzene and ether, said powder having a pH of 6.0 to 8.3, and ultraviolet absorptions of λ_{max}=265-275 nm, and a pharmaceutically acceptable carrier.

According to still another aspect of the present invention there is provided a method for treating a patient afflicted with inflammation, pain or allergic disease comprising administering a pharmaceutically effective amount of a water-soluble extract from animal tissue or animal cells which have been inoculated with a virus or a tumor

cultured cell strain to generate substances which inhibit the production of plasma kallikrein, said extract comprising 1 to 20 micrograms/mg of at least one silicon component calculated as silicon and having ultraviolet absorptions of λ_{max}=265-275 nm, wherein the color reactions of the extract are: a) positive for amino acids, sugars and phosphorus, and

b) negative for proteins and phenols, and wherein said at least one silicon component comprises at least one member selected from the group consisting of water-soluble silicic acids, water-soluble silicates, polymers of water soluble silicic acids, and polymers of water soluble silicates and wherein said water-soluble extract is admixed with a pharmaceutically acceptable carrier.

According to still another aspect of the present invention there is provided a method for treating a patient afflicted with inflammation, pain or allergic disease comprising administering a pharmaceutically effective amount of a water-soluble extract from an activated animal tissue, said extract comprising 1 to 20 micrograms/mg of at least one silicon component calculated as silicon and having ultraviolet absorptions of λ_{max}=265-275 nm, wherein the color reactions of the extract are: a) positive for amino acids, sugars and phosphorus, and b) negative for proteins and phenols and wherein said water-soluble extract is admixed with a pharmaceutically acceptable carrier.

The present invention will be further illustrated as hereunder.

The animal tissues used in the present invention are cultured tissues cultured cells or inflammatory tissues of human or animal origin which are infected with virus, or chorio-allantoic membranes of embryonated eggs infected with virus. Examples of the virus used for the activation of the animal tissues as a stressor are vaccinia virus, cowpox virus, variola virus, ectromelia virus, simian pox virus and

CLAIMS

1. A physiologically active substance which is extracted from an activated animal tissue comprising an amorphous and hygroscopic powder containing 1-20 micrograms/mg of at least one silicon component calculated as silicon, the powder being soluble in water, methanol and ethanol and being insoluble in benzene and ether, said powder having a pH of 6.0 to 8.3, and ultraviolet absorptions of λ_{max}=265-275 nm.

2. A substance as claimed in claim 1 wherein the color reactions of said powder are: a) positive for amino acids, sugars and phosphorus and b) negative for proteins and phenols.

3. A substance as claimed in claim 2 wherein said at least one silicon component comprises at least one member selected from the group consisting of water-soluble silicic acids, water-soluble silicates, polymers of water soluble silicic acids, and polymers of water soluble silicates.

4. A substance as claimed in claim 3 which contains 2 to 10 micrograms/mg of said at least one silicon component, calculated as silicon.

5. A substance as claimed in claim 3 which contains 5 to 14 micrograms/mg of said at least one silicon component, calculated as silicon.

6. A substance as claimed in claim 1 wherein said tissue is activated by inoculation with a virus.

7. A substance as claimed in claim 1 wherein said tissue is activated by inoculation with a tumor-cultured cell strain derived from human beings or other animals.

8. A substance as claimed in claim 1 wherein said activated tissue is a member selected from the group consisting of cultured tissues, cultured cells, and inflammatory tissues of human or animal origin which are injected with virus.

9. A pharmaceutical composition comprising a pharmaceutically effective amount of physiologically active substance which is extracted from an activated animal tissue, said substance comprising an amorphous and hygroscopic powder containing 1-20 micrograms/mg of at least one silicon component calculcated as silicon, the powder being soluble in water, methanol and ethanol and being insoluble in benzene and ether, said powder having a pH of 6.0 to 8.3, and ultraviolet absorptions of λ_{max}=265-275 nm, and a pharmaceutically acceptable carrier.

10. A pharmaceutical composition as claimed in claim 9 wherein said carrier is at least one member selected from the group consisting of distilled water, physiologically saline solution, Ringer's solution, plant oil, synthetic fatty acid glycerides, higher fatty acid esters, propylene glycol, lactose, mannitol, corn starch, crystalline cellulose, gum arabicum, gelatin, potato starch, carmerose, carmerose calcium, talc, and magnesium stearate.

11. A pharmaceutical composition as claimed in claim 9 which is a solid or semi-solid.

12. A pharmaceutical composition as claimed in claim 9 which is an aerosol.

13. A pharmaceutical composition as claimed in claim 9 wherein said animal tissue is selected from the group consisting of human hemocytes and placentae, kidney, skin, lung, testes, muscle, adrenal gland, thyroid gland, brain, nerve cells, and hemocytes.

14. A composition as claimed in claim 9 wherein the color reactions of said extract are: a) positive for amino acids, sugars and phosphorus and b) negative for proteins and phenols.

15. A method for treating a patient afflicted with inflammation, pain or allergic disease comprising administering a pharmaceutically effective amount of a water-soluble extract from animal tissue or animal cells which have been inoculated with a virus or a tumor cultured cell strain to generate substances which inhibit the production of plasma kallikrein, said extract comprising 1 to 20 micrograms/mg of at least one silicon component calculated as silicon and having ultraviolet absorptions of λ_{max}=265-275 nm, wherein the color reactions of the extract are: a) positive for amino acids, sugars and phosphorus, and b) negative for proteins and phenols, and wherein said at least one silicon component comprises at least one member selected from the group consisting of water-soluble silicic acids, water-soluble silicates, polymers of water soluble silicic acids, and polymers of water soluble silicates and wherein said water-soluble extract is admixed with a pharmaceutically acceptable carrier.

16. A method for treating a patient afflicted with inflammation, pain or allergic disease comprising administering a pharmaceutically effective amount of a water-soluble extract from an activated animal tissue, said extract comprising 1 to 20 micrograms/mg of at least one silicon component calculated as silicon and having ultraviolet absorptions of λ_{max}=265-275 nm, wherein the color reactions of the extract are: a) positive for amino acids, sugars and phosphorus, and b) negative for proteins and phenols and wherein said water-soluble extract is admixed with a pharmaceutically acceptable carrier.

17. A method as claimed in claim 16 wherein said carrier is at least one member selected from the group consisting of distilled water, physiologically saline solution, Ringer's solution, plant oil, synthetic fatty acid glycerides, higher fatty acid esters, propylene glycol, lactose, mannitol, corn starch, crystalline cellulose, gum arabicum, gelatin, potato starch, carmerose, carmerose calcium, talc, and magnesium stearate.

A NOVEL PHYSIOLOGICALLY ACTIVE SUBSTANCE

ABSTRACT

A novel physiologically active substance exhibiting a plasma kallikrein production inhibiting action, peripheral blood flow improving action and analgesic, antiinflammatory and antiallergic actions is offered.

The physiologically active substance of the present invention is prepared by activating various animals or animal tissues by means of inoculating virus or tumor cells which act as a stressor and then by extracting the effective factor from the activated tissues. The invention relates to a substance which exhibits a pharmacological action of inhibiting an activity for the plasma kallikrein production and recovers and normalizes the abnormal function which is resulted in the diseased state.

The physiologically active substance of the present invention exhibiting an excellent regulating activity for biofunctions has an action of recovering and normalizing the abnormal function of the living organisms in various diseased states and is quite useful as a pharmaceutical such as a peripheral blood flow improving agent, analgesic agent, antiinflammatory agent and antiallergic agent.