Human Kunitz-type Inhibitor with Enhanced Antifibrinolytic Activity

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Technology description

A human Kunitz-type inhibitor polypeptide with enhanced antifibrinolytic activity.
This novel polypeptide is structurally similar to the KD1 domain of human TFIP-2. This method allows the administration of an effective amount of polypeptide to a subject in need of treatment. In some instances, the polypeptide comprises a KD1 domain of human TFPI-2. While in other instances, the polypeptide comprises human TFPI-2, itself. The polypeptide can be administered in an amount which is effective to induce apoptosis in tumor cells.

Background

Bovine pancreatic trypsin inhibitor, known as aprotinin or Trasylol®, inhibits the degradation of fibrinogen by plasmin. Aprotinin therapy is associated with reduced risk of stroke in patients undergoing coronary artery bypass graft surgery and is widely used to reduce post-operative bleeding. Aprotinin, being of bovine origin, precipitates episodes of severe anaphylaxis in 0.5-1% of patients and an even larger percentage of patients who receive aprotinin a second time. The drug Trasylol®, which is given before coronary bypass surgery to prevent excessive blood loss, was taken off the market because of deaths due to hemorrhage compared with other blood-clotting drugs.
Proteinase inhibitors play a critical role in the regulation of several physiological processes such as blood coagulations, complement fixation, fibrinolysis, and fertilization. Most of these inhibitors are proteins having characteristic polypeptide scaffolds, and are grouped into a number of families including the Kunitz family. The Kunitz-type family comprises serine proteinase inhibitors that include one or more Kunitz-type inhibitory domains. The Kunitz-type family also includes tissue factor pathway inhibitor (TFIP) and type-2 tissue factor inhibitor (TFIP-2). Recent studies have shown that the down-regulation of TFPI-2 by tumor cells plays a significant role in the invasive properties of human gliomas. Plasmin is known to degrade fibrinogen after surgery. Aprotinin is widely used to inhibit the activity of plasmin, however it can cause anaphylaxis. Therefore, there is still a need for improved formulas that have antifibrinolytic activity without the negative side effects.

Technology Description

Researchers at the University of New Mexico have developed a human Kunitz-type inhibitor polypeptide with enhanced antifibrinolytic activity. This novel polypeptide is structurally similar to the KD1 domain of human TFIP-2. This method allows the administration of an effective amount of polypeptide to a subject in need of treatment. In some instances, the polypeptide comprises a KD1 domain of human TFPI-2. While in other instances, the polypeptide comprises human TFPI-2, itself. The polypeptide can be administered in an amount which is effective to induce apoptosis in tumor cells. Related to technology 2004-045

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Application area

Therapeutic applications
Prevention of thrombosis following surgery

Institution

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