necessary to take advantage of the hemostatic effect of self-assembling peptides to a level allowing their clinical application.
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DISCLOSURE OF THE INVENTION
PROBLEMS TO BE SOLVED BY THE INVENTION
[0022]

The objective of the present invention is to provide a self-assembling peptide tissue occluding agent that can effectively occlude sites of tissue damage in large mammals including humans and that does not carry the risk of infection by viruses and the like, as well as a method for use of the same.

MEANS FOR SOLVING THE PROBLEMS
[0023]

The present inventors have completed this invention upon finding that a tissue occluding effect equivalent to or greater than that of existing tissue occluding agents is exhibited when a self-assembling peptide hydrogel utilized as a scaffold for cell culture is applied for tissue occlusion. It has been a noted issue that simply applying aqueous peptide solutions to body fluid leakage sites does not provide a sufficient tissue occluding effect. As a result of diligent research, however, it was found that a sufficient tissue occluding effect and biological safety can be achieved by removing excess body fluid from body fluid leakage sites.
[0024]

Specifically, ~~the invention relates to~~in one aspect, the present invention provides a tissue occluding agent comprising a peptide, wherein the peptide has an amino acid sequence as set forth in SEQ ID NO: 2. Also disclosed is a tissue occluding agent containing a peptide, wherein the peptide is an amphiphilic peptide having 8-200 amino acid residues with the hydrophilic amino acids and hydrophobic amino acids alternately bonded, and is a self-assembling peptide exhibiting a β-structure in aqueous solution in the presence of physiological pH and/or a cation.
[0025]

In this tissue occluding agent, the peptide is preferably a self-assembling peptide having a repeating sequence which is a sequence comprising arginine, alanine, aspartic acid and alanine, a sequence comprising isoleucine, glutamic acid, isoleucine and lysine, or a sequence comprising lysine, leucine, aspartic acid and leucine, and more preferably it is a self-assembling peptide comprising the amino acid sequence listed as SEQ ID NO: 1, SEQ ID NO: 2 or SEQ ID NO: 3.
[0026]

The tissue occluding agent also preferably comprises small molecular drugs to prevent hemolysis, inflammation and infection.

[0027]

The small molecular drugs are preferably selected from the group consisting of glucose, saccharose, purified saccharose, lactose, maltose, trehalose, dextran, iodine, lysozyme chloride, dimethylisopropylazulene, tretinoin tocoferil, povidone iodine, alprostadil alfadex, anise alcohol, isoamyl salicylate, α,α-dimethylphenylethyl alcohol, bacdanol, helional, sulfazin silver, bucladesine sodium, alprostadil alfadex, gentamycin sulfate, tetracycline hydrochloride, sodium fusidate, mupirocin calcium hydrate and isoamyl benzoate.

[0028]

In another aspect, there is provided a hemostatic agent for hemorrhage of blood in a condition of reduced clotting function induced by addition of an anticoagulant, comprising the tissue occluding agent as described herein.

In yet another aspect there is provided a hemostatic agent for a hemorrhaging wound surface of a parenchymal organ, comprising the tissue occluding agent as described herein.

In yet another aspect there is provided a hemostatic agent for arterial hemorrhage and phleborrhagia, comprising the tissue occluding agent as described herein.

In yet another aspect there is provided an agent for preventing bile leakage from the gall bladder or bile duct, comprising the tissue occluding agent as described herein.

In yet another aspect there is provided an agent for preventing hemorrhage or air leakage from the lungs, comprising the tissue occluding agent as described herein.

In yet another aspect there is provided a mucosal tissue infusion for elevating an excision site in endoscopic demucosation, the infusion comprising the tissue occluding agent as described herein.

In yet another aspect there is provided an agent for preventing hemorrhage and body fluid leakage from an excision site in a method of excising a mucosal tissue section that has been elevated by infusion of a liquid into the mucosal tissue, the agent comprising the tissue occluding agent as described herein.

In yet another aspect there is provided a hemostatic agent applicable for transcatheter application for hemostasis from an excision site in endoscopic demucosation, the agent comprising the tissue occluding agent as described herein.

In yet another aspect there is provided an arteriovenous occluding agent for arteriovenous occlusion or a varix sclerotherapy agent for varix sclerotherapy, comprising the tissue occluding agent as described herein.

The ~~invention~~disclosure also relates to agents comprising the aforementioned tissue occluding agent, which are hemostatic agents for hemorrhage of blood that have reduced coagulating power due to addition of anticoagulants, hemostatic agents for hemorrhage wound surfaces on parenchymal organs, hemostatic agents for arterial hemorrhage and phleborrhagia, inhibitors of bile leakage from the gall bladder or bile duct, inhibitors of hemorrhage or air leakage from the lungs, hemostatic agents or transcatheter application during endoscopic demucosation, infusions for mucosal tissue for swelling of excision sites, inhibitors of hemorrhage and body fluid leakage from excision sites in methods of excising mucosal tissue resections that have been swelled by infusion of liquids into the mucosal tissue, or arteriovenous occluding agents in arteriovenous occlusion or varix sclerotherapy agents used in varix sclerotherapy. Anticancer agents and/or contrast agents may also be added to the arteriovenous occluding agent or varix sclerotherapy agent.

EFFECT OF THE INVENTION

[0029]

The self-assembling peptide as the major component in the tissue occluding agent of the invention can also serve as a scaffold for migrating cells in addition to its role as a occluding agent, thus allowing it to have a higher curative effect after surgery instead of simple occlusion. In addition, the tissue occluding agent of the invention has improved adhesion to tissue when excess body fluid has been removed from a body fluid leakage site (for example, when it has been applied to a hemorrhage arrest site where hemorrhage has been stopped), and thus exhibits an adequate tissue occluding effect with biological safety.

[0030]

TISSUE OCCLUDING AGENT

ABSTRACT

There is provided a bioabsorbable peptide tissue occluding agent that can be applied to large mammals including humans, the peptide tissue occluding agent being obtained by artificial synthesis to avoid concerns of infection by viruses and the like.

The tissue occluding agent contains a peptide, wherein the peptide is an amphiphilic peptide having 8-200 amino acid residues with the hydrophilic amino acids and hydrophobic amino acids alternately bonded, and is a self-assembling peptide exhibiting a β-structure in aqueous solution in the presence of physiological pH and/or a cation.

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