SUMMARY

In one aspect, there is provided a sterile, ready-to-use, flowable haemostatic composition comprising: a soluble haemostatic agent comprising a plurality of carriers and a plurality of fibrinogen-binding peptides immobilised to each carrier; a biocompatible liquid; and particles of a biocompatible cross-linked polysaccharide suitable for use in haemostasis and which are insoluble in the biocompatible liquid.

In another aspect, there is provided a composition described herein for use as a medicament.

In another aspect, there is provided a composition described herein for use in the treatment of bleeding, or in the treatment of a wound.

In another aspect, there is provided use of a composition described herein in the manufacture of a medicament for use in the treatment of bleeding, or in the treatment of a wound.

In another aspect, there is provided a method of making a sterile, ready-to-use, flowable haemostatic composition, which comprises: mixing together a biocompatible liquid, a soluble haemostatic agent, and particles of a biocompatible cross-linked polysaccharide suitable for use in haemostasis and which are insoluble in the biocompatible liquid, wherein the soluble haemostatic agent comprises a plurality of carriers and a plurality of fibrinogen-binding peptides immobilised to each carrier; and sterilizing the composition.

DETAILED DESCRIPTION

According to the invention there is provided a haemostatic composition comprising: a soluble haemostatic agent comprising a plurality of carriers and a plurality of fibrinogen-binding peptides immobilised to each carrier; a biocompatible liquid; and particles of a biocompatible cross-linked polysaccharide suitable for use in haemostasis and which are insoluble in the biocompatible liquid. According to certain embodiments of the invention, the compositions are ready-to-use, flowable, haemostatic compositions.

It has been found that the haemostatic agents in compositions of the invention are surprisingly resistant to sterilization, particularly steam sterilization, or dry-heat sterilization. Consequently, compositions of the invention may be sterilized using conventional sterilization methods without significant loss of haemostatic activity. This is an important advantage because it allows the compositions to be provided as hydrated, sterile, ready-to-use, flowable haemostatic compositions. Conventional gelatin-based haemostats comprising thrombin are not stable when heat or steam sterilised in hydrated, ready-to-use form.

The term "haemostatic" is used herein to mean the ability to stop or minimize bleeding.

The term "biocompatible" is used herein to mean that the material is compatible with living tissue by not being toxic or injurious and not causing immunological rejection. The material should preferably meet the criteria in standard # ISO 10993-1 promulgated by the International Organization for Standardization (NAMSA, Northwood, Ohio).

The term "flowable" is used herein to mean that the compositions flow when subjected to stresses above a threshold level, for example when extruded through an orifice or cannula or when packed into a delivery site using a spatula. The threshold stresses are typically in the range from 3×10^4 Pa to 5×10^5 Pa. The compositions, however, will remain generally immobile when subjected to stresses below the threshold level. A flowable composition is generally able to conform to irregular wound geometries at a target site to which the composition is delivered.

The haemostatic agent, liquid and insoluble particles may be combined and mixed under conditions effective to provide a substantially homogeneous haemostatic composition comprising a continuous, biocompatible liquid phase, comprising the particles substantially homogenously dispersed throughout the liquid phase.

32. A composition according to any preceding claim, having a solids content of 1-70%, or 5-20%, by weight of the composition.

33. A composition according to any of claims 1 to 31, wherein a weight ratio of the particles to the liquid is from 1:1 to 1:12, or from 1:3 to 1:8.

34. A composition according to any preceding claim, wherein the composition is transparent.

35. A composition according to any of claims 1 to 34 for use as a medicament.

36. A composition according to any of claims 1 to 34 for use in the treatment of bleeding, or in the treatment of a wound.

37. Use of a composition according to any of claims 1 to 34 in the manufacture of a medicament for use in the treatment of bleeding, or in the treatment of a wound.

38. A method of making a sterile, ready-to-use, flowable haemostatic composition, which comprises:

mixing together a biocompatible liquid, a soluble haemostatic agent, and particles of a biocompatible cross-linked polysaccharide suitable for use in haemostasis and which are insoluble in the biocompatible liquid, wherein the soluble haemostatic agent comprises a plurality of carriers and a plurality of fibrinogen-binding peptides immobilised to each carrier; and

sterilizing the composition.

39. A method according to claim 38, wherein the composition is sterilized by steam sterilization, or by dry-heat sterilization.

40. A method according to claim 38 or 39, wherein the liquid, the agent, and the particles are mixed under conditions effective to form a continuous liquid phase comprising

the particles substantially homogeneously dispersed throughout the liquid phase, thereby forming a substantially homogeneous haemostatic composition.

41. A method according to any of claims 38 to 40, which further comprises centrifuging the mixture to remove air bubbles from the mixture.

42. A method according to any of claims 38 to 40, wherein the biocompatible liquid and the particles are mixed together before addition of the soluble haemostatic agent.

43. A method according to claim 42, which further comprises centrifuging the mixture of the biocompatible liquid and the particles to remove air bubbles from the mixture before addition of the soluble haemostatic agent.