A hemostatic composition for effecting hemostasis at a hemorrhaging site comprises a hemostatically effective amount of cationic substance and a wax base, wherein the cationic substance is substantially uniformly dispersed in the bone wax base. The method of preparing the hemostatic composition includes admixing an aqueous solution of a cationic substance and a bone wax, and freeze-drying the mixture to remove substantially all of the water to yield a viscous water soluble composition of fine particles of cationic which is substantially uniformly dispersed throughout the bone wax base. The method for effecting hemostasis comprises making the hemostatic composition and applying a hemostatically effective amount of the hemostatic composition to the hemorrhaging site.
HEMOSTATIC BONE WAX COMPOSITION

REFERENCE TO RELATED APPLICATION
[0001] This application is a continuation in part of U.S. patent application Ser. No. 10/008,052, filed Nov. 13, 2001, the disclosure of which is incorporated herein by reference.

FIELD OF THE INVENTION
[0002] The invention relates to hemostatic compositions useful for surgical applications. More particularly, the invention relates to a hemostatic composition for application to bleeding bone surfaces.

BACKGROUND OF THE INVENTION
[0003] Puncture of blood vessels is a necessary stage in many of the minimally invasive approaches to diagnosis and treatment, including interventional radiology and cardiology. Therefore, a need to create hemostasis as rapidly as possible following the procedure becomes an important priority.

[0004] The cationic substance may be a high molecular weight cationic polyelectrolyte. Generally, the cationic polymer is derived from animals (sea life) or plants (fungi, polysaccharides), or synthesized by various processes.

[0005] Suitable cationic substances are generally available in two forms, i.e., dry powder or an aqueous solution. In a dry powder form, the cationic substance is used by tapping the cationic particles out from a container onto the hemorrhaging site. The dry powder cationic substance is not easily handled and applied during surgery because it is difficult to quickly measure out the desired amount when a hemorrhaging site is discovered. Cationic substance used in aqueous solution has the disadvantage of diminishing the potency of the cationic substance by dilution. Further, aqueous cationic substance solutions are not stable due to the denaturation and autolysis of the cationic substance in solution. It is therefore an object of the present invention to provide a hemostatically effective, convenient, and storage stable form of cationic substance ideally suited for surgical use.

SUMMARY OF THE INVENTION
[0006] The present invention provides a hemostatic composition, which comprises a hemostatically effective cationic substance and a wax base, wherein the cationic substance is substantially uniformly dispersed in the wax base.

[0007] Many hemostasis methods have been utilized or attempted, including suturing-based devices, collagen plugs, pressure applying devices, and the like. The situation is complicated further by the use of anticoagulants in these procedures, which prolongs clotting times. Substances such as heparin, aspirin, coumadin, and other anticoagulants are used with regularity and affect the normal blood coagulation cascade. The use of cationic substances in flocculation and coagulation in non-medical situations such as water treatment, paper production, industrial sludge treatment, and the like has been effectively used in the past and is well documented. The method of action is by precipitating, coagulating or flocculating suspended particles which are negatively charged by virtue of using positively charged materials, which attract the oppositely charged ions.

[0008] It has been clearly demonstrated that the charge on blood cells and components (platelets, etc.) is negative. By using a positively charged biocompatible substance, it is possible to agglomerate these cells creating coagulation through a system other than by virtue of the normal clotting cascade. Innocuous polymers are positively charged (cationic substances) as the initiator of coagulation in clinical situations. Additionally, positive charges can be applied via iontophoretic methods using electrode pads and positively charged treatment sites to accomplish the same thing.

[0009] The use of a positive charge administered by either cationic substances or by iontophoretic means to quickly create a coagulation process and hemostasis until the normal clotting cascade can take over. This can occur even in the face of significant anticoagulation since the process is ionic and not effected by the anticoagulants, which operate on the normal blood cascade. This approach can be revolutionary in the after treatment of patients with minimally invasive or invasive procedures since rapid hemostasis and mobilization of the patient are desirable endpoints.

[0010] The cationic substance can be incorporated into many forms, such as woven and non-woven pads, fibers, gels, pastes, waxes, foams, sprays, liquids of varying viscosities, packings, membranes, sheets, and the like. Additionally, these forms can be incorporated and utilized with iontophoretic types of equipment that create a positive charge at the bleeding site to effect coagulation.

[0011] Utilizing colloidal chemistry for affecting coagulation ionically in suspensions or colloidal substance by providing cationic charges, has enormous value in the diagnosis and treatment of conditions such as cardiovascular disease, interventional radiological procedures, and the like. The cationic charge can be provided by a substance with a positively charged surface, or electronically by utilizing electrophoretic type equipment and electrode pads specifically designed to be disposable, conductive and sterile, designed to fit the required anatomical site. Many cationic substances are available, such as polymers, polysaccharides and starches, aluminum salts, magnesium salts, natural polymers such as chitosan, and the like.

[0012] The use of ionic charges to create hemostasis is a new and important process in the treatment of disease processes. This novel approach can be administered by applying sterile, biocompatible, positively charged materials directly in contact with the blood column, accompanied by pressure, or provided electronically by utilizing controlled direct current on the positive side with iontophoretic type approaches and specialty constructed, disposable, sterile electrodes to the bleeding site.

[0013] In accordance with purposes of the invention, as embodied and fully described herein, the invention comprises a hemostatic composition comprising a hemostatically effective amount of cationic substance in a wax base. The cationic substance may be folded in as a powder or may be dissolved in biocompatible solutes and added mechanically as a solution. Preferably, a cationic substance powder is dissolved in a mixture of water and mechanically mixed with a wax base in appropriate ratios and the mixture is dried, preferably freeze-dried to remove the water leaving the particles of cationic substance substantially uniformly dispersed in the wax base.

[0014] The invention also comprises a process for preparing a hemostatic composition comprising the steps of:
admixing an aqueous solution of cationic substance and a wax base, and freeze-drying the mixture to remove substantially all of the water to yield a viscous water soluble wax of cationic substance.

[0015] The invention further comprises a method for reducing bleeding at a hemorrhaging site by applying a cationic substance wax composition which comprises a hemostatically effective amount of cationic substance in a wax base to the hemorrhaging site of a mammal. The cationic substance may be applied in combination with a fibrous gauze material or by itself in wax form to the hemorrhaging site.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0016] Reference will now be made in detail to preferred embodiments of the invention.

[0017] The hemostatic cationic wax composition of the present invention provides convenient ready to use hemostatically effective amounts of cationic substance for application to a hemorrhaging surface of a bone. A cationic substance composition is homogeneously dispersed throughout a wax base and remains storage stable until it is ready for use.

[0018] The cationic substance is a high molecular weight cationic polymer. The cationic polymer may be derived and purified by various processes. The hemostatic properties of related cationic substances have been known for years and prior arts exist for the use of these substances in bleeding situations. The nature of their use in the majority of prior art and expired patents was as a powder, a liquid or as a coated paper or saturated gauze pad.

[0019] Already-to-use wax form of the present invention is advantageous over solution forms of cationic substances which must be reconstituted from dry cationic substance powder prior to use. Additionally, cationic substance solutions generally have a low viscosity and a low potency due to their dilute nature. Aqueous solutions of cationic substance are frequently applied in conjunction with, and absorbed on, a coated paper, or saturated gauze dressing because of its low viscosity and potency. The hemostatic cationic substance wax composition of the present invention has a viscosity and potency which is high enough to permit its hemostatically effective use by a surgeon by dipping of a gloved finger into the hemostatic cationic substance wax composition to draw a portion of that composition and placing the drawn portion over the bleeding site.

[0020] The cationic substance wax composition requires no pre-preparation; it is non-toxic and absorbable by a mammalian body. It can be supplied in a sterile convenient to use delivery system such as a wax tube, jar or containers. The cationic substance wax composition is anti-microbial as well due to the nature of these cationic substances.

[0021] In accordance with the purposes of the invention, as embodied and fully described herein, one embodiment of the invention comprises a mixture of a base of bone wax and a hemostatically effective amount of a cationic substance.

[0022] Bone wax is a sterile beeswax preparation. It is sometimes formulated as a semi-synthetic mixture of beeswax and softening agents (such as isopropyl palmitate) to make a more pliable product. The product is used to control local bleeding. In neurosurgical and orthopedic procedures, it is used to control bleeding from raw edges of bone.

[0023] The use of bone wax has some drawbacks in that it must be used sparingly as it may inhibit osteogenesis and limit the healing process by mechanical means. Also studies have shown that there is occasionally mild reaction as well as infection as result of too profuse an application of the wax. Mixing the hemostatic cationic substance into the bone wax can enhance the hemostatic effect of bone wax while retaining its mechanical tamponading ability and allows the good features of the bone wax to be retained while minimizing the amount of the material required to stop the bleeding. By creating the hemostatic composition of the present invention that retains the mechanical tamponade qualities and adherence characteristics of bone wax, while adding a powerful natural hemostatic polymer, the amount of the composition needed is minimized, thereby limiting complications and the known drawbacks of bone wax.

[0024] In this invention, a hemostatic cationic substance is formulated together with a bone wax and is packaged sterile in collapsible tubes or containers. Preferably, the hemostatic cationic substance is in the range 30-60% of the weight of the final wax mixture, but other ranges can be used. The agent may be dissolved in the wax or mechanically mixed.

[0025] Applying the hemostatic composition in the form of wax to a dressing or directly to the bleeding wound or structure (e.g., bone), presents the substance to the bleeding surface or blood column more easily. Furthermore, the composition in form of wax adapts itself to the surface shape so that greater approximation is accomplished. It may be most efficiently utilized with constant pressure for several minutes after application. The coagulum that forms as a result of the cationic clumping of platelets and blood cells is in addition to the natural clotting cascade and enhances hemostasis to controllable levels. It is also known that may of these cationic polyelectrolytes are anti-microbial as well, enhancing the clinical applications.

[0026] In the above embodiments, the hemostatic agent is preferably a cationic biopolymer of glucosamine. The cationic biopolymer of glucosamine may be in one or more of the following forms: poly-D-glucosamine; an acetate salt of poly-N-acetylg glucosamine; an acetate salt of poly-D-glucosamine; poly-D-glucosaminide and poly-D-glucosamine; an acetate salt of poly-N-acetylg glucosamine and poly-D-glucosamine; an acetate salt of poly-N-acetylg glucosamine and an acetate salt of poly-D-glucosamine; and poly-N-acetylg glucosamine and an acetate salt of poly-D-glucosamine. In forms including an acetate salt, the application surface is water soluble. Acidic environments other than an acetate salt, such as lactic acid, can also be incorporated as part of the biopolymer of glucosamine.

[0027] In a preferred form, the cationic biopolymer of glucosamine is derived from chitosan, which is a collective term applied to deacetylated chitins in various stages of deacetylation and depolymerization. Chitosan is the structural polymer of the exo-skeleton of arthropods and cell walls of fungi, and is composed of poly-N-Acetyl glucosamine units. These are linked by Beta 1-4 glycosidic bonds into a linear polymer containing 2,000 to 3,000 units.

[0028] The invention may be embodied in other specific forms without departing from the spirit or essential chara-
teristics thereof. The present embodiments are therefore to be considered in all respects illustrative and not restrictive, the scope of the invention being indicated by the appended claims rather than by the foregoing description, and all changes which come within the meaning and range of equivalency of the claims are therefore intended to be embraced therein.

What is claimed is:

1. A hemostatic composition comprising:
   a hemostatically effective amount of hemostatic cationic substance; and
   a base in a form of wax, and wherein said hemostatic cationic substance is substantially uniformly dispersed in said base.
2. The composition of claim 1, wherein the hemostatic cationic substance comprises a biopolymer of glucosamine.
3. The composition of claim 2, wherein the biopolymer of glucosamine is poly-N-acetylgucosamine.
4. The composition of claim 2, wherein the biopolymer of glucosamine is poly-D-glucosamine.
5. The composition of claim 2, wherein the biopolymer of glucosamine is an acetate salt of poly-N-acetylgucosamine.
6. The composition of claim 2, wherein the biopolymer of glucosamine is an acetate salt of poly-D-glucosamine.
7. The composition of claim 2, wherein the biopolymer of glucosamine is poly-N-acetylgucosamine and poly-D-glucosamine.
8. The composition of claim 2, wherein the biopolymer of glucosamine is an acetate salt of poly-N-acetylgucosamine and poly-D-glucosamine.
9. The composition of claim 2, wherein the biopolymer of glucosamine is an acetate salt of poly-N-acetylgucosamine and an acetate salt of poly-D-glucosamine.
10. The composition of claim 2, wherein the biopolymer of glucosamine is poly-N-acetylgucosamine and an acetate salt of poly-D-glucosamine.
11. The composition of claim 1, wherein said base is a water-soluble.
12. The composition of claim 1, wherein said base is a water-soluble.
13. The composition of claim 1 further includes an anti-microbial material.
14. A method for making a hemostatic composition comprising:
   mixing a hemostatically effective amount of hemostatic cationic substance and a base, wherein said base is in a form of wax.
15. The method of claim 14, wherein the hemostatic cationic substance comprises a biopolymer of glucosamine.
16. The method of claim 15, wherein the biopolymer of glucosamine is poly-N-acetylgucosamine.
17. The method of claim 15, wherein the biopolymer of glucosamine is poly-D-glucosamine.
18. The method of claim 15, wherein the biopolymer of glucosamine is an acetate salt of poly-N-acetylgucosamine.
19. The method of claim 15, wherein the biopolymer of glucosamine is an acetate salt of poly-D-glucosamine.
20. The method of claim 15, wherein the biopolymer of glucosamine is poly-N-acetylgucosamine and poly-D-glucosamine.
21. The method of claim 15, wherein the biopolymer of glucosamine is an acetate salt of poly-N-acetylgucosamine and poly-D-glucosamine.
22. The method of claim 15, wherein the biopolymer of glucosamine is an acetate salt of poly-N-acetylgucosamine and an acetate salt of poly-D-glucosamine.
23. The method of claim 15, wherein the biopolymer of glucosamine is poly-N-acetylgucosamine and an acetate salt of poly-D-glucosamine.
24. The method of claim 14, wherein said base is bone wax.
25. The method of claim 14, wherein said base is water-soluble.
26. The method of claim 14 further includes a step of mixing an anti-microbial material in said composition.
27. A method for effecting hemostatic composition at a hemorrhaging site in a mammal comprising:
   A) forming a hemostatic composition by mixing a hemostatically effective amount of hemostatic cationic substance and a base, wherein said base is in form of wax; and
   B) applying a hemostatic effective amount of said hemostatic composition to the hemorrhaging site of the mammal.
28. The method of claim 27, wherein the hemostatic cationic substance comprises a biopolymer of glucosamine.
29. The method of claim 28, wherein the biopolymer of glucosamine is poly-N-acetylgucosamine.
30. The method of claim 28, wherein the biopolymer of glucosamine is poly-D-glucosamine.
31. The method of claim 28, wherein the biopolymer of glucosamine is an acetate salt of poly-N-acetylgucosamine.
32. The method of claim 28, wherein the biopolymer of glucosamine is an acetate salt of poly-D-glucosamine.
33. The method of claim 28, wherein the biopolymer of glucosamine is poly-N-acetylgucosamine and poly-D-glucosamine.
34. The method of claim 28, wherein the biopolymer of glucosamine is an acetate salt of poly-N-acetylgucosamine and poly-D-glucosamine.
35. The method of claim 28, wherein the biopolymer of glucosamine is an acetate salt of poly-N-acetylgucosamine and an acetate salt of poly-D-glucosamine.
36. The method of claim 28, wherein the biopolymer of glucosamine is poly-N-acetylgucosamine and an acetate salt of poly-D-glucosamine.
37. The method of claim 27, wherein said base is bone wax.
38. The method of claim 27 further includes maintaining pressure for a predetermined time on the hemorrhaging site after applying said hemostatic composition to the hemorrhaging site of the mammal.