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(54) Title: A METHOD FOR TREATING CONTAMINATED PRODUCTS AND ARTICLES (57) Abstract A method for the denaturation of proteins and/or DNA present in products derived from animals or on the surface of an article, comprising treating the animal derived product or the surface of the article with a denaturing agent in an amount effective to denature the protein and/or DNA.		

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A Method For Treating Contaminated Products and Articles.

Technical Field

The present invention relates to a method for treating products and articles contaminated or potentially contaminated with contagious pathogenic agents.

Background Art

There is a high level of awareness throughout the world that human illness and fatality can result from a variety of sources including the consumption of contaminated animal derived products wherein the animal has become the host for a contagious pathogenic agent and from infections obtained from articles contaminated with contagious pathogenic agents. When an animal infected with a contagious pathogenic agent is slaughtered the pathogenic agent is present in all the cellular body parts which are usually utilised for human use. The end products of the animal used for human consumption, such as meat and gelatine, therefore, can be potentially contaminated with contagious pathogenic agents.

Similarly, surfaces of articles, such as surgical apparatus, which come into contact with a contagious pathogenic agent may be the source of infection to other animals/humans if they are not suitably decontaminated and sterilised. The deadly brain disease Creutzfeldt-Jakob disease (CJD), the human form of Bovine Spongiform Encephalopathy (BSE), is an infection which is known to be present in both the central nervous system and throughout the lymph tissue of victims. At present, there is no effective way to sterilise surgical apparatus contaminated with prions that cause the disease CJD. There is concern that the temperatures routinely used to sterilise surgical instruments in hospitals may help to spread CJD. Further, increasing the temperatures of the autoclave used to disinfect instruments may actually make it harder to destroy the CJD prions.

Pathogens are disease causing parasites which include DNA and/or proteins in their structural make-up. They cause disease by invading and multiplying in the living tissue of a host cell. Contagious pathogenic agents such as very small viruses, plasmids or prions have been known to cause brain diseases such as, "Mad Cow" disease (BSE), Creutzfeldt-Jacob disease (CJD) or Scrapie. Prions have been defined as proteins which have become sticky clumps and cause neurological havoc and are thought to be the cause

of the brain diseases. Recent research postulates that prions may play a role in reproduction complimentary or additional to genes.

Native globular proteins and solutions of double helical DNA undergo significant changes in a number of physical properties when subjected to:
5 heat; extremes of pH; exposure to strong solutions of amides such as urea or urea derivatives such as guanidine hydrochloride; organic solvents; radiation; enzymes; and detergents. This physical change is called denaturation. Denaturation of proteins and DNA yields unfolded, random conformations of their corresponding polypeptide and DNA chains and results in the loss of
10 the proteins biological activity.

The bonds which are affected by the denaturation process include hydrogen bonds; hydrophobic bonds; salt bridges or ionic bonds between groups which are positively and negatively charged; and intramolecular bonds such as are found in cross linkages due to the disulfide bond groups of
15 cystine.

Urea and guanidine are examples of denaturation agents. Although the mechanism of action of these denaturing agents is not fully understood, it is believed that they disrupt non-covalent interactions. In proteins, polypeptide chains devoid of cross-links usually assume a random-coil confirmation in 8
20 M urea or 6 molar guanidine hydrochloride, as evidenced by physical properties such as viscosity and optical rotary spectra. These compounds break hydrogen bonds in the protein, presumably by forming hydrogen bonds of its own due to its peptide like character.

Disulfides bonds can be cleaved reversibly by reduction with a reagent
25 such as beta-mercaptoethanol. However, the protein ribonuclease cannot be readily reduced by beta-mercaptoethanol unless the protein is partially unfolded by denaturing agents such as urea or guanidine hydrochloride.

The contagious pathogenic agents causing brain diseases such as "Mad Cow" disease, Creutzfeldt-Jacob disease or Scrapie are not destroyed by
30 commonly used methods such as heat or radiation treatment.

There is clearly a need for a method of treating animal derived products such as gelatine or other polypeptide containing products derived from animals which are contaminated or potentially contaminated with infectious pathogenic agents. As the gelatine or other polypeptide product
35 will ultimately be consumed by an animal or human, they are required in their purest uncontaminated state.

There is also clearly a need for a method of treating surfaces of articles which are contaminated or potentially contaminated with infectious pathogenic agents.

5 The present inventor has surprisingly found that this can be achieved by treating the animal derived product or the surface of an article with denaturing agents such as urea derivatives.

Throughout this specification, unless the context requires otherwise, the word "comprise", or variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated element, integer or step, or
10 group of elements, integers or steps, but not the exclusion of any other element, integer or step, or group of elements, integers or steps.

Disclosure of the Invention

In a first aspect, the present invention relates to a method for the denaturation of proteins and/or DNA present in gelatine or other polypeptide
15 products derived from animals, comprising treating the gelatine or other polypeptide product with a denaturing agent in an amount effective to denature the proteins and/or DNA without substantially affecting the gelatine or other polypeptide product.

In a second aspect, the present invention relates to a method of
20 treating gelatine or other polypeptide products derived from animals potentially contaminated with contagious pathogenic agents, comprising treating the gelatine or other polypeptide products with a denaturing agent in an amount effective to denature proteins and/or DNA of the contagious pathogenic agent without substantially affecting the gelatine or other
25 polypeptide products.

In a third aspect, the present invention relates to use of a denaturing agent for the denaturation of proteins and/or DNA present in gelatine or other polypeptide products derived from animals, wherein the gelatine or other polypeptide product is treated with the denaturing agent in an amount
30 effective to denature the proteins and/or DNA without substantially affecting the gelatine or other polypeptide product.

In a fourth aspect, the present invention is directed to the use of a denaturing agent for treating gelatine or other polypeptide products derived from animals potentially contaminated with contagious pathogenic agents,
35 wherein the gelatine or other polypeptide products are treated with a denaturing agent in an amount effective to denature proteins and/or DNA of

the contagious pathogenic agent without substantially affecting the gelatine or other polypeptide products.

5 In a fifth aspect, the present invention relates to a denaturing agent when used to denature proteins and/or DNA present in gelatine or other polypeptide products derived from animals, wherein the gelatine or other polypeptide product is treated with the denaturing agent in an amount effective to denature the proteins and/or DNA without substantially affecting the gelatine or other polypeptide product.

10 The other polypeptide products derived from animals may be animal extracts or meat for animal or human consumption.

15 In a sixth aspect, the present invention relates to a method for the denaturation of proteins and/or DNA present on the surface of an article, comprising treating the surface of the article with a denaturing agent in an amount effective to denature the proteins and/or DNA of the contagious pathogenic agent without substantially affecting the surface of the article.

20 In a seventh aspect, the present invention relates to a method of treating a surface of an article potentially contaminated with contagious pathogenic agents, comprising treating the surface of the article with a denaturing agent in an amount effective to denature proteins and/or DNA of the contagious pathogenic agent without substantially affecting the surface of the article.

25 In an eighth aspect, the present invention relates to use of a denaturing agent for the denaturation of proteins and/or DNA present on the surface of an article, wherein the surface of the article is treated with the denaturing agent in an amount effective to denature the proteins and/or DNA without substantially affecting the surface of the article.

30 In a ninth aspect, the present invention is directed to the use of a denaturing agent for treating a surface of an article potentially contaminated with contagious pathogenic agents, wherein the surface of the article is treated with a denaturing agent in an amount effective to denature proteins and/or DNA of the contagious pathogenic agent without substantially affecting the surface of the article.

35 In a tenth aspect, the present invention relates to a denaturing agent when used to denature proteins and/or DNA present on the surface of an article, wherein the surface of the article is treated with the denaturing agent

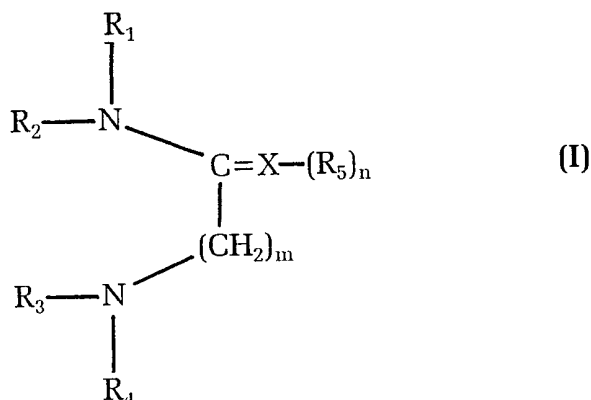
in an amount effective to denature the proteins and/or DNA without substantially affecting the surface of the article.

The surface of the article to be treated may be soft or hard. Soft surfaces includes surfaces which are malleable and have little or no resistance to pressure or weight and includes natural and synthetic fabrics. Hard surfaces include surfaces which are firm or rigid and include steel and steel alloys such as stainless steel. Preferably, the surface of the article to be treated is the stainless steel surface of a surgical apparatus.

Generally, the proteins and/or DNA to be denatured are contained in or derived from contagious pathogenic agents. The contagious pathogenic agents may be very small viruses, plasmids or prions.

Preferably, the properties of the animal derived products or the surface of the article which are contaminated with the contagious pathogenic agent are not substantially affected when treated with the denaturing agent, such that the denaturing agent reacts with the proteins and/or DNA of the contagious pathogen rather than the animal product or the surface of the article. Varying factors such as the concentration of the denaturing agent and the time of reaction between the denaturing agent and the contaminated animal product or surface of article may be used to control the reaction between the denaturing agent and the animal derived product and surface of the article.

Preferably, the denaturing agent is the urea analogue compound according to formula (I):



wherein,

X is selected from nitrogen or oxygen;

R_5 is selected from the group including hydrogen or an alkyl group optionally substituted with one or more amine groups and wherein when X is oxygen, $n = 0$;

$m = 0$ to 1

5 R_1 , R_2 , R_3 and R_4 may each represent hydrogen, lower alkyl, carboxyl or an alkyl carboxyl group optionally substituted with one or more amine groups and wherein either R_1 , or R_2 may be taken together with either R_3 or R_4 as $-\text{CO}-\text{CH}_2-$ to form a five-membered ring;

or its salt derivative thereof.

10 The salt derivative of Formula (I) is preferably selected from the chloride, nitrate or aluminium sulphate salt.

Preferably, the denaturing agent is non-toxic and selected from the group consisting of urea, guanidine, L(+)-Arginine, creatine and creatinine or salts thereof. More preferably, the urea derivative is guanidine or guanidine hydrochloride.

15 Preferably, the animal derived product or surface of the article contaminated (or possibly contaminated) with the contagious pathogenic agent is treated with a 0.1% w/v up to a saturated solution, preferably a 5 to 10% w/v solution, of the denaturing agent. The solution may be based on organic or non-organic solvents which dissolve the denaturing agent.

20 Preferably, the solvent is selected from an alcohol, such as ethanol, water or an aqueous alcoholic mix. The animal derived product contaminated with a contagious pathogenic agent may be treated in a dry state, as a gel or in a liquid, such as water, which is preferably heated to a temperature of over

25 40°C .

In one embodiment, a dry animal derived product or surface of the article contaminated with a contagious pathogenic agent is washed with an alcoholic solution of the denaturing agent such that the denaturing agent does not dissolve the animal derived product or the surface of the article but

30 allows reaction of the guanidine with the contagious pathogenic agent. The contagious pathogen may be in the form of CJD prions or BSE prions. Preferably, the denaturing agent is guanidine or its hydrochloride salt and the solvent is ethanol, water or a water-ethanol mix.

Following, treatment of the animal derived product in dry or solution

35 form with a solution of the denaturing agent, the solvent may be removed by usual methods such as reduced pressure evaporation or drying at

approximately 50°C to 80°C. The remaining animal derived product and the residual denaturing agent may be treated in any one of the following manners:

- 5 (a) the gelatine may be further purified by extraction into water, washing with ethanol and drying;
- (b) the denaturing agent, provided it is non-toxic, can be left in the animal derived product (guanidine and its salts, for example, are generally non-toxic);
- 10 (c) the amount of denaturing agent contaminating the animal derived product can be reduced by drying the gelatine and further purifying it by usual methods such as centrifugation, spray drying, adsorption etc;
- (d) most of or all of the denaturing agent may be eliminated from the animal derived product by using additional method steps, such as, the utilisation of different solubilities or adsorption methods;
- 15 (e) a solution of the animal derived product or dry gelatine still containing a denaturing agent such as guanidine and or its salts can be treated in an autoclave type container with heat under pressure (equivalent to 160°C at normal pressure) to convert
- 20 guanidine into ammonia (which evaporates or can be evaporated) and melamine. The melamine which is almost insoluble in water can be separated (eg by filtration or centrifugation), from a solution of the animal derived product in a non-organic solvent.

25 The treated animal derived product can be further purified by usual processes, such as extraction into water, washing with ethanol and drying.

The surface of articles contaminated or potentially contaminated with BSE prions, such as the surface of stainless steel surgical instruments, may be treated by immersing the article in a 0.1% w/v up to a saturated solution, preferably a 5 to 10% w/v solution, of the denaturing agent in a solvent such as an aqueous or alcoholic solution. Preferably, the article is immersed in 5

30 to 10% w/v guanidine or guanidine hydrochloride in either ethanol or water for one hour at approximately 40-50°C or in an autoclave for 10-20 minutes at 130-140°C. Any other sterilising processes can be additionally applied in the conventional manner.

35 The denaturing process renders the pathogen harmless. As indicated above, the denaturing agent and the solvent may be removed by separating

the treated material from the solution. The treated material may then be washed with pure solvent such as water or alcohol followed by drying. If the utilised denaturing agent is guanidine or its salts and a method such as autoclaving has been used which brings the conditions to an equivalent of 160°C or more the guanidine is converted to melamine and ammonia. Both can be easily separated from the treated material by washing or a similar process. The denatured and rendered harmless pathogen no longer needs to be separated from the treated material.

In order that the present invention may be more clearly understood, preferred forms will be described with reference to the following examples.

Modes for Carrying Out the Invention

Example 1: Treatment of Gelatine

Gelatine is water soluble at > 40°C and is a mix of proteins derived by partial hydrolysis of animal collagen. According to the invention, gelatine contaminated with a contagious pathogenic agent, such as BSE prions, may be treated according to any one of the following methods:

- (1) A 10 micron to 200 micron layer of gelatine contaminated with BSE prions may be treated with 10% w/v guanidine hydrochloride in water.

The solvent from the mixture may then be removed under reduced pressure evaporation to leave the decontaminated gelatine and residual guanidine hydrochloride. The gelatine may be further purified by extraction into water, washing with ethanol and drying.

- (2) A 300 micron to 1 mm layer of gelatine contaminated with BSE prions may be treated with 5% w/v guanidine in ethanol.

The solvent from the mixture may be removed by reduced pressure evaporation. The gelatine residue may be further purified by extraction into water, washing with ethanol and drying.

The gelatine may be further purified by centrifugation to reduce the contamination by guanidine.

- (3) A solution of 20% w/v gelatine in water at $> 40^{\circ}\text{C}$ may be treated with 10% w/v guanidine hydrochloride in water.

5 The solvent from the mixture may be removed by reduced pressure evaporation or drying at 50°C to 80°C .

Most of or all of the guanidine hydrochloride may be eliminated from the gelatine by utilising the different solubilities of the two substances.
10 The resulting gelatine residue may be further purified by washing with ethanol and drying; or

- (4) A gel of 30% w/v gelatine in water at room temperature may be treated with 15% w/v guanidine hydrochloride in water.

15 The gelatine solution or the dry gelatine still containing guanidine hydrochloride may be treated in an autoclave type container with heat under pressure (equivalent to 160°C at normal pressure) to convert guanidine into ammonia and melamine. The ammonia may be
20 evaporated. The melamine may be separated by filtration from a solution of gelatine in a non-organic solvent. The resulting gelatine residue may be further purified by washing with ethanol and drying.

Example 2: Treatment of other animal derived article

25 The treatment of other material (besides gelatine) derived from animal material contaminated with a contagious pathogenic agent, such as, animal extracts or meat, can be carried out according to any one of methods 1 to 4 outlined in Example 1 although the chosen method may depend on the different solubilities and adsorption characteristics of the material to be
30 treated.

Example 3: Treatment of surface of surgical instruments:

According to the invention, surfaces of articles contaminated with a contagious pathogenic agent, such as BSE or CJD prions, may be treated
35 according to either one of the following methods:

(1) Stainless steel surgical instruments contaminated or potentially contaminated with BSE or CJD prions were immersed in 10% w/v guanidine in water for 10 hours at 50°C.

5 (2) Stainless steel surgical instruments contaminated or potentially contaminated with BSE or CJD prions were immersed and autoclaved in 5% w/v guanidine hydrochloride in ethanol for 20 minutes at 135°C.

10 In both (1) and (2), the surgical instruments were removed and rinsed in water. Additionally, in (2), the instruments may be further sterilised in the conventional manner, such as, in an autoclave.

It will be appreciated by persons skilled in the art that numerous variations and/or modifications may be made to the invention as shown in the specific embodiments without departing from the spirit or scope of the invention as broadly described. The present embodiments are, therefore, to
15 be considered in all respects as illustrative and not restrictive.

CLAIMS

1. A method for the denaturation of proteins and/or DNA present in gelatine or other polypeptide products derived from animals, comprising treating the gelatine or other polypeptide products with a denaturing agent in an amount effective to denature the proteins and/or DNA without substantially affecting the gelatine or other polypeptide product.
2. A method according to claim 1 wherein the proteins and/or DNA to be denatured are contained in or derived from contagious pathogenic agents.
3. A method according to claim 2 wherein the contagious pathogenic agents are viruses, plasmids or prions.
4. A method for the denaturation of proteins and/or DNA present on the surface of an article, comprising treating the surface of the article with a denaturing agent in an amount effective to denature the proteins and/or DNA without substantially affecting the surface of the article.
5. A method according to claim 4 wherein the proteins and/or DNA to be denatured are contained in or derived from contagious pathogenic agents.
6. A method according to claim 5 wherein the contagious pathogenic agents are viruses, plasmids or prions.
7. A method of treating gelatine or other polypeptide products derived from animals potentially contaminated with contagious pathogenic agents, comprising treating the gelatine or other polypeptide products with a denaturing agent in an amount effective to denature proteins and/or DNA of the contagious pathogenic agent without substantially affecting the gelatine or other polypeptide products.
8. A method of treating a surface of an article potentially contaminated with contagious pathogenic agents, comprising treating the surface of the article with a denaturing agent in an amount effective to denature proteins and/or DNA of the contagious pathogenic agent without substantially affecting the properties of the surface of the article.
9. A method according to any one of claims 2, 3 or 7 wherein the contagious pathogenic agent is BSE prions.
10. A method according to any one of claims 5, 6 or 8 wherein the contagious pathogenic agent is selected from BSE or CJD prions.
11. A method according to any one of claims 4, 5, 6, 8 or 10 wherein the surface of the article is soft.

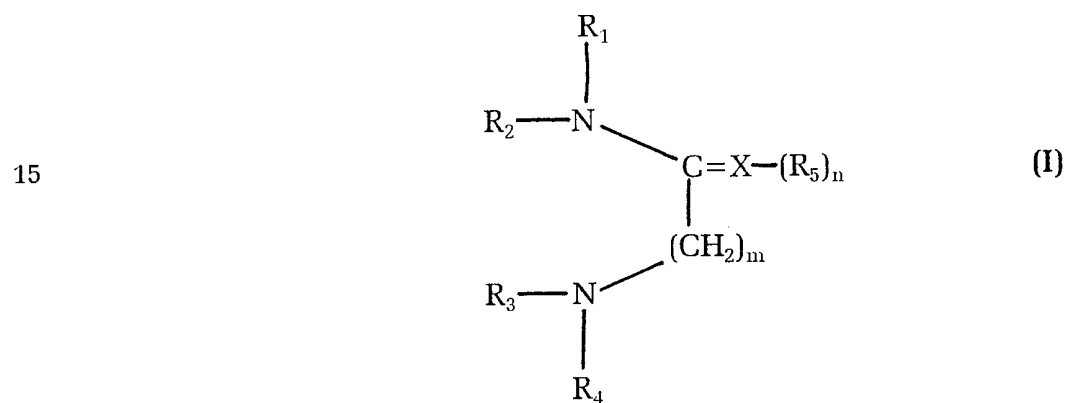
12. A method according to any one of claims 4, 5, 6, 8 or 10 wherein the surface of the article is hard.

13. A method according to any one of claims 4, 5, 6, 8 or 10 wherein the surface of the article is the surface of a stainless steel surgical apparatus.

5 14. A method according to any one of claims 1, 2, 3, 7 or 9 wherein the polypeptide products derived from animals are animal extracts or meat for human or animal consumption

15. A method according to any one of claims 1 to 14 wherein the denaturing agent is the urea analogue compound according to formula (I):

10



20

wherein,

X is selected from nitrogen or oxygen;

R₅ is selected from the group including hydrogen or an alkyl group optionally substituted with one or more amine groups and wherein when X is oxygen, n = 0;

25

m=0 to 1;

R₁, R₂, R₃ and R₄ may each represent hydrogen, lower alkyl, carboxyl or an alkyl carboxyl group optionally substituted with one or more amine groups and wherein either R₁, or R₂ may be taken together with either R₃ or R₄ as -CO-CH₂- to form a five-membered ring;

30

or a salt thereof.

16. A method according to claim 15 wherein the salt of the urea analogue compound is a chloride, nitrate or aluminium sulphate salt.

17. A method according to claim 15 wherein the urea derivative is selected from the group consisting of urea, guanidine, guanidine hydrochloride,

35

L(+)-Arginine, creatine and creatinine.

18. A method according to claim 15 wherein the denaturing agent is guanidine or guanidine hydrochloride.

19. A method according to claim 15 wherein the denaturing agent is in a solution containing from 0.1% w/v up to a saturated solution, preferably a 5 to 10% w/v solution, of denaturing agent.

20. A method according to claim 19 wherein the denaturing agent is in a solvent selected from an alcoholic solution, water or an aqueous alcoholic mix.

21. Use of a denaturing agent for the denaturation of proteins and/or DNA present in gelatine or other polypeptide products derived from animals, wherein the gelatine or other polypeptide product is treated with the denaturing agent in an amount effective to denature the proteins and/or DNA of the contagious pathogenic agent without substantially affecting the gelatine or other polypeptide product.

22. Use according to claim 21 wherein the proteins and/or DNA to be denatured are contained in or derived from contagious pathogenic agents.

23. Use according to claim 22 wherein the contagious pathogenic agents are viruses, plasmids or prions.

24. Use of a denaturing agent for the denaturation of proteins and/or DNA present on the surface of an article, wherein the surface of the article is treated with the denaturing agent in an amount effective to denature proteins and/or DNA without substantially affecting the surface of the article.

25. Use according to claim 24 wherein the proteins and/or DNA to be denatured are contained in or derived from contagious pathogenic agents.

26. Use according to claim 25 wherein the contagious pathogenic agents are viruses, plasmids or prions.

27. Use of a denaturing agent for treating gelatine or other polypeptide products derived from animals potentially contaminated with contagious pathogenic agents, wherein the gelatine or other polypeptide products is treated with a denaturing agent in an amount effective to denature proteins and/or DNA of the contagious pathogenic agent without substantially affecting the gelatine or other polypeptide products.

28. Use of a denaturing agent for treating a surface of an article potentially contaminated with contagious pathogenic agents, wherein the surface of the article is treated with a denaturing agent in an amount effective to denature

proteins and/or DNA of the contagious pathogenic agent without substantially affecting the surface of the article.

29. Use according to any one of claims 22, 23 or 27 wherein the contagious pathogenic agent is BSE prions.

5 30. Use according to any one of claims 25, 26 or 28 wherein the contagious pathogenic agent is selected from BSE or CJD prions.

31. Use according to any one of claims 24, 25, 26, 28 or 30 wherein the surface of the article is soft.

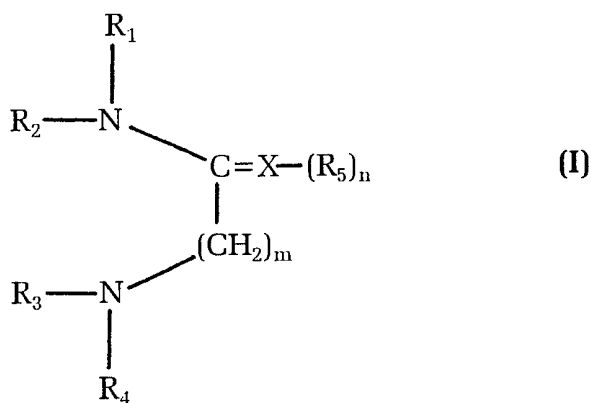
10 32. Use according to any one of claims 24, 25, 26, 28 or 30 wherein the surface of the article is hard.

33. Use according to any one of claims 24, 25, 26, 28 or 30 wherein the surface of the article is the surface of a stainless steel surgical apparatus.

34. Use according to any one of claims 21, 22, 23, 27 or 29 wherein the polypeptide products derived from animals are animal extracts or meat for
15 human or animal consumption

35. Use according to any one of claims 21 to 34 wherein the denaturing agent is the urea analogue compound according to formula (I):

20



25

wherein,

30

X is selected from nitrogen or oxygen;

R_5 is selected from the group including hydrogen or an alkyl group optionally substituted with one or more amine groups and wherein when X is oxygen, $n = 0$;

$m = 0$ to 1;

R₁, R₂, R₃ and R₄ may each represent hydrogen, lower alkyl, carboxyl or an alkyl carboxyl group optionally substituted with one or more amine groups and wherein either R₁, or R₂ may be taken together with either R₃ or R₄ as -CO-CH₂- to form a five-membered ring;

5 or a salt thereof.

36. Use according to claim 35 wherein the salt of the urea analogue compound is a chloride, nitrate or aluminium sulphate salt.

37. Use according to claim 35 wherein the urea derivative is selected from the group consisting of urea, guanidine, guanidine hydrochloride,

10 L(+)-Arginine, creatine and creatinine.

38. Use according to claim 35 wherein the denaturing agent is guanidine or guanidine hydrochloride.

39. Use according to claim 35 wherein the denaturing agent is in solution containing from 0.1% w/v up to a saturated solution, preferably a 5 to 10%
15 w/v solution, of denaturing agent.

40. Use according to claim 39 wherein the denaturing agent is in a solvent selected from an alcoholic solution, water or an aqueous alcoholic mix.

41. A denaturing agent when used to denature proteins and/or DNA present in gelatine or other polypeptide products derived from animals, wherein the gelatine or other polypeptide product is treated with the denaturing agent in an amount effective to denature the proteins and/or DNA without substantially affecting the gelatine or other polypeptide product.

42. A denaturing agent according to claim 41 wherein the proteins and/or DNA to be denatured are contained in or derived from contagious pathogenic
20 agents.

43. A denaturing agent according to claim 42 wherein the contagious pathogenic agents are viruses, plasmids or prions.

44. A denaturing agent when used to denature proteins and/or DNA present on the surface of an article, wherein the surface of the article is treated with the denaturing agent in an amount effective to denature the proteins and/or DNA without substantially affecting the surface of the article.

45. A denaturing agent according to claim 44 wherein the proteins and/or DNA to be denatured are contained in or derived from contagious pathogenic agents.

46. A denaturing agent according to claim 45 wherein the contagious pathogenic agents are viruses, plasmids or prions.

47. A denaturing agent according to any one of claims 42 or 43 wherein the contagious pathogenic agent BSE prions.

48. A denaturing agent according to any one of claims 45 or 46 wherein the contagious pathogenic agent is selected from BSE or CJD prions.

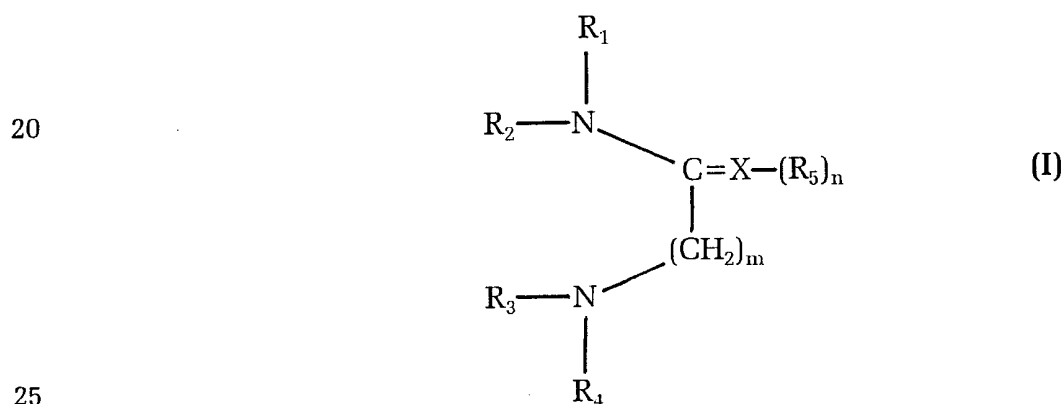
5 49. A denaturing agent according to any one of claims 44, 45, 46 or 48 wherein the surface of the article is soft.

50. A denaturing agent according to any one of claims 44, 45, 46 or 48 wherein the surface of the article is hard.

51. A denaturing agent according to any one of claims 44, 45, 46 or 48
10 wherein the surface of the article is the surface of a stainless steel surgical apparatus.

52. A denaturing agent according to any one of claims 41, 42, 43 or 47 wherein the polypeptide products derived from animals are animal extracts or meat for human or animal consumption

15 53. A denaturing agent according to any one of claims 41 to 52 wherein the denaturing agent is the urea analogue compound according to formula (I):



wherein,

X is selected from nitrogen or oxygen;

30 R₅ is selected from the group including hydrogen or an alkyl group optionally substituted with one or more amine groups and wherein when X is oxygen, n = 0;

m=0 to 1;

R₁, R₂, R₃ and R₄ may each represent hydrogen, lower alkyl, carboxyl or an alkyl carboxyl group optionally substituted with one or more amine

groups and wherein either R₁, or R₂ may be taken together with either R₃ or R₄ as -CO-CH₂- to form a five-membered ring;
or a salt thereof.

5 54. A denaturing agent according to claim 53 wherein the salt of the urea analogue compound is a chloride, nitrate or aluminium sulphate salt.

55. A denaturing agent according to claim 53 wherein the urea derivative is selected from the group consisting of urea, guanidine, guanidine hydrochloride,

L(+)-Arginine, creatine and creatinine.

10 56. A denaturing agent according to claim 53 wherein the denaturing agent is guanidine or guanidine hydrochloride.

57. A denaturing agent according to claim 53 wherein the denaturing agent is in solution containing from 0.1% w/v up to a saturated solution, preferably a 5 to 5% w/v solution, of denaturing agent.

15 ~~58~~. A denaturing agent according to claim 57 wherein the denaturing agent is in a solvent selected from an aqueous alcoholic solution, water or a non-organic solution.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU 99/00249

A. CLASSIFICATION OF SUBJECT MATTERInt Cl⁶: A61L 2/16; 2/18; A23J 3/04, 3/06, 3/12, 3/30, 3/32; C09H 3/02, 5/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A61L 2/16; 2/18; A23J 3/04, 3/06, 3/12, 3/30, 3/32; C09H 3/02, 5/00

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

WPAT: IPC and (polypeptid: or protein: or collagen: or gelatin: or dna or deoxyribo:)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 374 063 (CONSOLAZIO et al.) 15 February 1983 whole specification	1-3,7,14,19- 23,27,34,39-43
X	WO 97/28192 (DOILLON Charles et al.) 7 August 1997 whole specification	1-3,7,14,19- 23,27,34,39-43
X	WO 95/18529 (ORGANOGENESIS, INC.) 13 July 1995 whole specification	1-3,7,14,19- 23,27,34,39-43

☒ Further documents are listed in the
continuation of Box C☒ See patent family annex

* Special categories of cited documents:	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent but published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search
20 May 1999Date of mailing of the international search report
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INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU 99/00249

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 742 018 (COLLAGEN CORPORATION) 13 November 1996 whole specification	1-3,7,14,19- 23,27,34,39-43
X	EP 0 748 632 (BIOLAND S.a.r.l.) 18 December 1996 whole specification	1-3,7,14,19- 23,27,34,39-43
A	WO 95/09657 (IMMUNO AG) 13 April 1995 whole specification	1-3,7,14,19- 23,27,34,39-43
X	AU 50453/90 (628432) (SIMMONS, Paul) 9 August 1990 whole specification	4-6,8,11- 13,19-20,24- 26,28,31- 33,44-46,49- 51

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.
PCT/AU 99/00249

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report				Patent Family Member			
US	4374063						
WO	97/28192	AU	14353/97	CA	2243193	EP	877761
WO	95/18529	CA	2179017	EP	738106	US	5460962
EP	742018	CA	2172918	JP	8308912	US	5756678
EP	748632	FR	2735372	US	5723012	US	5725579
		CA	2110527	CN	1090206	EP	603920
		FR	2699408	JP	6218036		
AU	50453/90	CA	1337329	EP	457805	GB	9113078
		GB	2245171	HU	57609	US	5441723
		WO	90/08559	US	5145663	US	5405602
		US	5637307	AU	44061/93	EP	647141
		WO	94/00157	AU	37217/93	WO	93/16737
		AU	73298/94	GB	9600476	GB	2294639
		MX	9401009	NZ	269419	WO	95/02393

END OF ANNEX