WHAT IS CLAIMED IS:

1. An albumin-binding arginine deiminase fusion protein comprising a first portion comprising one or two components selected from an albumin-binding domain, an albumin-binding peptide or an albumin-binding protein(s) fused to a second portion comprising arginine deiminase to form the albumin-binding arginine deiminase fusion protein such that the albumin-binding arginine deiminase fusion protein retains the activity of arginine deiminase and is also able to bind serum albumin.

2. An albumin-binding arginine deiminase fusion protein according to claim 1 wherein the two components are the same.

3. An albumin-binding arginine deiminase fusion protein according to claim 1 wherein the two components are different.

4. An albumin-binding arginine deiminase fusion protein according to claim 1 wherein the albumin-binding domain is SEQ ID NO. 46, 47, 48, 49 or an active portion thereof.

5. An albumin-binding arginine deiminase fusion protein according to claim 1 wherein the albumin binding peptide is SEQ ID NO. 46, 47, 48, 49 or an active portion thereof.

6. An albumin-binding arginine deiminase fusion protein according to claim 1 wherein the albumin binding protein is SEQ ID NO. 46, 47, 48, 49 or an active portion thereof.

7. An albumin-binding arginine deiminase fusion protein according to claim 1 wherein the fusion includes one or more linker molecule(s).

8. An albumin-binding arginine deiminase fusion protein according to claim 7 wherein the linker molecule includes a sequence selected from SEQ ID NO. 50, 51, 52, 53, or serine-glycine-serine (SGS) amino acid sequence.

9. An albumin-binding arginine deiminase fusion protein according to claim 1 further comprising at least one of Poly-N or a His tag.

10. An albumin-binding arginine deiminase fusion protein according to claim 1 wherein the fusion includes a remaining portion of an intein-mediated protein ligation between the first portion and the second portion.

11. An albumin-binding arginine deiminase fusion protein according to claim 10 wherein the intein-mediated protein includes a chitin binding domain.

12. An albumin-binding arginine deiminase fusion protein according to claim 1 wherein the arginine deiminase is selected from arginine deiminase produced from a *Mycoplasma*, *Lactococcus*, *Pseudomonas, Streptococcus, Escherichia*, *Mycobacterium* or *Bacillus* microorganism.

13. An albumin-binding arginine deiminase fusion protein according to claim 12 wherein the arginine deiminase is produced from *Mycoplasma arginini*, *Lactococcus lactis*, *Bacillus licheniformis, Bacillus cereus*, *Mycoplasma arthritidis, Mycoplasma hominis, Streptococcus pyogenes, Streptococcus pneumonia, Streptococcus pneumoniae, Mycobacterium tuberculosis, Pseudomonas plecoglossicida, Pseudomonas putida, Pseudomonas aeruginosa* or a combination thereof.

14. An albumin-binding arginine deiminase fusion protein according to claim 1 wherein the arginine deiminase includes a sequence selected from SEQ ID NO. 36, 37, 38, 39, 40, 41, or 43.

15. An albumin-binding arginine deiminase fusion protein according to claim 1 wherein the fusion protein is formed by reacting the arginine deiminase having a N-terminal cysteine residue with a reactive thioester at C-terminus of the albumin-binding domain so that the arginine deiminase and the albumin-binding domain are linked by a covalent bond.

16. An albumin-binding arginine deiminase fusion protein according to claim 1 wherein the fusion protein is formed by reacting the albumin-binding domain having a N-terminal cysteine residue with a reactive thioester at C-terminus of the arginine deiminase so that the arginine deiminase and the albumin-binding domain are linked by a covalent bond.

17. An albumin-binding arginine deiminase fusion protein according to claim 1 wherein the fusion protein is formed by using SEQ ID NOS. 42 and 43 and by reacting the arginine deiminase having a N-terminal cysteine residue with a reactive thioester at C-terminus of the albumin-binding domain so that the arginine deiminase and the albumin-binding domain are linked by a covalent bond.

18. Use of the albumin-binding arginine deiminase fusion protein according to any one of claims 1 to 17 in preparation of a medicament for treating a cancer in a patient comprising administering a clinically effective amount of the fusion protein to the patient to reduce the availability of circulating arginine.

19. The use according to claim 18 wherein the cancer is pancreatic cancer, leukemia, head and neck cancer, colorectal cancer, lung cancer, breast cancer, liver cancer, nasopharyngeal cancer, esophageal cancer, prostate cancer, stomach cancer or brain cancer.

20. Use of the albumin-binding arginine deiminase fusion protein according to any one of claims 1 to 17 in preparation of a medicament for treating arginine-dependent diseases in a patient comprising administering a clinically effective amount of the fusion protein to the patient to reduce the availability of circulating arginine.

21. A method of making the albumin-binding arginine deiminase fusion protein of claim 1 comprising constructing a fusion gene coding for the albumin-binding arginine deiminase fusion protein, inserting the fusion gene into a vector, inserting the vector into a host organism and expressing a protein including the albumin-binding arginine deiminase fusion protein of claim 1.

22. The method of making the albumin-binding arginine deiminase fusion protein according to claim 21 further comprising purifying the fusion protein.

23. The method of making the albumin-binding arginine deiminase fusion protein according to claim 22 wherein the purifying is performed by chromatography.

24. The method of making the albumin-binding arginine deiminase fusion protein according to claim 22 wherein the purifying is performed from soluble fractions of crude proteins.

25. The method of making the albumin-binding arginine deiminase fusion protein according to claim 22 wherein the purifying is performed from insoluble fractions of crude proteins.

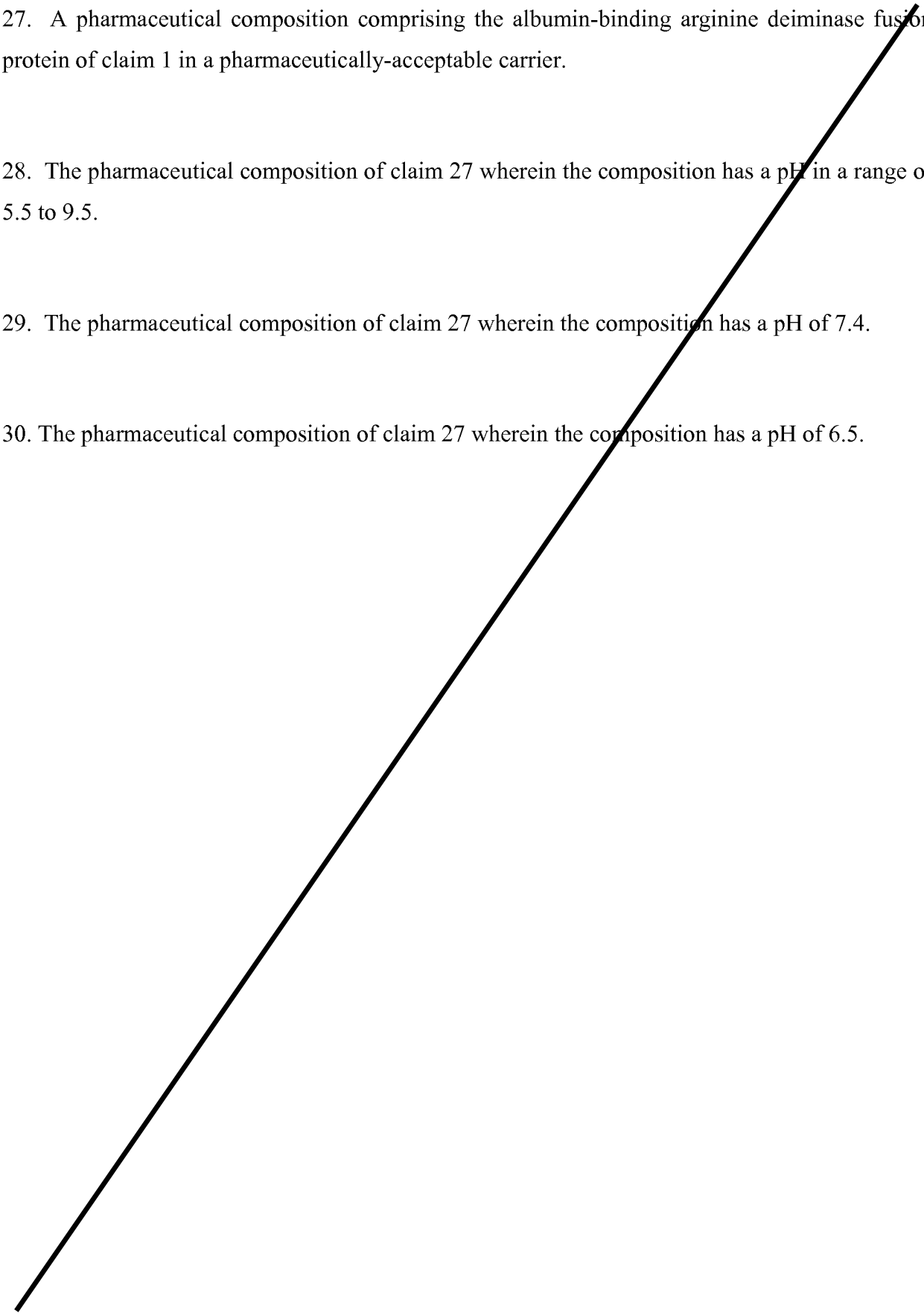
26. A method of making the albumin-binding deiminase fusion protein of claim 1 by intein mediated protein ligation between the albumin-binding domain, albumin-binding peptide or albumin-binding protein(s) and the second portion comprising arginine deiminase.

27. A pharmaceutical composition comprising the albumin-binding arginine deiminase fusion protein of claim 1 in a pharmaceutically-acceptable carrier.

28. The pharmaceutical composition of claim 27 wherein the composition has a pH in a range of 5.5 to 9.5.

29. The pharmaceutical composition of claim 27 wherein the composition has a pH of 7.4.

30. The pharmaceutical composition of claim 27 wherein the composition has a pH of 6.5.



WHAT IS CLAIMED IS:

1. An albumin-binding arginine deiminase fusion protein comprising a first portion comprising one or two components selected from an albumin-binding domain, an albumin-binding peptide or an albumin-binding protein(s) fused to a second portion comprising arginine deiminase to form the albumin-binding arginine deiminase fusion protein, and one or more linker molecules; the first portion being positioned far from active site of the second portion by said linker molecule such that the albumin-binding arginine deiminase fusion protein retains the activity of arginine deiminase and binds serum albumin with neither function of one portion of the fusion protein being interfered with by the other portion of the fusion protein, wherein pegylation of said arginine deiminase is avoided, and wherein the albumin-binding arginine deiminase fusion protein comprises a sequence selected from SEQ ID NO: 36, 37, 38, 39, 40, or 41.

2. The albumin-binding arginine deiminase fusion protein of claim 1 wherein the two components of the first portion are the same.

3. The albumin-binding arginine deiminase fusion protein of claim 1 wherein the two components of the first portion are different.

4. The albumin-binding arginine deiminase fusion protein of claim 1 wherein the albumin-binding domain is SEQ ID NO: 46, 47, 48, or 49.

5. The albumin-binding arginine deiminase fusion protein of claim 1 wherein the albumin binding peptide is SEQ ID NO: 46, 47, 48, or 49.

6. The albumin-binding arginine deiminase fusion protein of claim 1 wherein the albumin binding protein is SEQ ID NO: 46, 47, 48, or 49.

7. The albumin-binding arginine deiminase fusion protein of claim 1 wherein the linker molecule comprises a sequence selected from SEQ ID NO: 50, 51, 52, 53, or serine-glycine-serine (SGS) amino acid sequence.

8. The albumin-binding arginine deiminase fusion protein of claim 1 further comprising at least one of Poly-N or a His tag.

9. The albumin-binding arginine deiminase fusion protein of claim 1 wherein the fusion comprises a remaining portion of an intein-mediated protein ligation between the first portion and the second portion.

10. The albumin-binding arginine deiminase fusion protein of claim 9 wherein the intein-mediated protein comprises a chitin binding domain.

11. The albumin-binding arginine deiminase fusion protein of claim 1 wherein the arginine deiminase is selected from arginine deiminase produced from a *Mycoplasma*, *Lactococcus*, *Pseudomonas, Streptococcus, Escherichia, Mycobacterium* or *Bacillus* microorganism.

12. The albumin-binding arginine deiminase fusion protein of claim 11 wherein the arginine deiminase is produced from *Mycoplasma arginini, Lactococcus lactis, Bacillus licheniformis, Bacillus cereus, Mycoplasma arthritidis, Mycoplasma hominis, Streptococcus pyogenes,*

Streptococcus pneumoniae, Mycobacterium tuberculosis, Pseudomonas plecoglossicida, Pseudomonas putida, Pseudomonas aeruginosa or a combination thereof.

13. The albumin-binding arginine deiminase fusion protein of claim 1 wherein the fusion protein is formed by reacting the arginine deiminase having a N-terminal cysteine residue with a reactive thioester at C-terminus of the albumin-binding domain so that the arginine deiminase and the albumin-binding domain are linked by a covalent bond.

14. The albumin-binding arginine deiminase fusion protein of claim 1 wherein the fusion protein is formed by reacting the albumin-binding domain having a N-terminal cysteine residue with a reactive thioester at C-terminus of the arginine deiminase so that the arginine deiminase and the albumin-binding domain are linked by a covalent bond.

15. The albumin-binding arginine deiminase fusion protein of claim 1 wherein the fusion protein is formed by using SEQ ID NO: 42 and 43 and by reacting the arginine deiminase having a N-terminal cysteine residue with a reactive thioester at C-terminus of the albumin-binding domain so that the arginine deiminase and the albumin-binding domain are linked by a covalent bond.

16. A pharmaceutical composition comprising the albumin-binding arginine deiminase fusion protein of claim 1 in a pharmaceutically-acceptable carrier.

17. The pharmaceutical composition of claim 16 wherein the composition has a pH in a range of 5.5 to 9.5.

18. The pharmaceutical composition of claim 16 wherein the composition has a pH of 7.4.

19. The pharmaceutical composition of claim 16 wherein the composition has a pH of 6.5.

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