chemical modifications, including inter- or intramolecular polymerization, oxidation, complex formation, and/or cleavage by non-specific proteinases.

It is believed that the major physiological function of API is the inhibition of neutrophil elastase, cathepsin G, and proteinase 3. The API produced in individuals with PiZ API deficiency is functionally active, although there may be a decrease in its specific elastase inhibitory capacity. The predominant site of API synthesis is the liver, however, it is also synthesized in extrahepatic cell types including macrophages, intestinal epithelial cells and intestinal Paneth cells.

The pathogenesis of lung injury in API deficiency is attributable to the marked reduction in available API activity. API has been found to constitute greater than 90% of the neutrophil elastase inhibitor activity in pulmonary alveolar lavage fluid. Thus, it appears that the destructive lung disease seen in many individuals with API deficiency is due to a perturbation in the net balance between elastase and API within the lungs. The uninhibited activity of neutrophil elastase, cathepsin G, and proteinase 3, in turn, results in slow destruction of the connective tissue integrity of the lungs. This destruction of connective tissue leads to over distension and a reduction in the retractive force of the lungs which results in decreased expiratory airflow. Smoking exacerbates the problem by causing oxidative inactivation of what API is present.

At present, treatment options for individuals with pathologies associated with API deficiency are limited. Liver disease associated with API deficiency has been treated by orthotopic liver transplantation. Somatic gene therapy to replace the defective API gene has been discussed, but has yet to be successfully used.

There remains a need, therefore, for API compositions that are stable and that provide desirable API plasma bioavailability levels following administration to a subject.

SUMMARY ~~OF THE INVENTION~~

In one aspect, there is provided a composition comprising:

(a) an alpha 1-proteinase inhibitor (API); and

(b) at least one amino acid, wherein the at least one amino acid is present in the composition in a total amino acid amount of 0.01 M to 3 M such that the API retains at least 50% of its activity when the composition is exposed to a temperature for a period of at least 6 months, wherein the composition does not contain a sugar or contains a sugar in a total amount of less than 20% w/v.

In another aspect, there is provided a kit comprising the composition as defined herein as a pharmaceutical composition suitable for intravenous administration.

There is now provided, in one embodiment~~aspect~~, a composition comprising: (a) an alpha 1-proteinase inhibitor (API); and (b) at least one amino acid.

In another embodiment~~aspect~~, the present disclosure~~invention~~ provides methods for preparing the composition.

In other embodiment~~aspects~~, kits comprising the composition are provided.

We claim:

1. A composition comprising:

(a) an alpha 1-proteinase inhibitor (API); and

(b) at least one amino acid, wherein the at least one amino acid is present in the composition in a total amino acid amount of 0.01 M to 3 M such that the API retains at least 50% of its activity when the composition is exposed to a temperature for a period of at least 6 months,

wherein the composition does not contain a sugar or contains a sugar in a total amount of less than 20% w/v.

2. The composition of claim 1, wherein the temperature is 5 °C to 40 °C.

3. The composition of claim1, wherein the at least one amino acid is a neutral or a hydrophilic amino acid.

4. The composition of claim 1, wherein the at least one amino acid is selected from the group consisting of: alanine, threonine, serine, hydroxyproline, glycine, proline, leucine, and histidine.

5. The composition of claim 1, wherein the amino acid is alanine.

6. The composition of claim 1 further comprising one or more excipients.

7. The composition of Claim 6, wherein the one or more excipients is selected from the group consisting of: sucrose, mannitol, glycerol, sorbitol, dextran, trehalose, hydroxyethyl starch (HES), and 1,2-propanediol.

8. The composition of claim 1, wherein the composition further comprises a pharmaceutically acceptable carrier.

9. The composition of claim 1, wherein the composition is suitable for intravenous administration to a subject.

10. The composition of claim 1, wherein the at least one amino acid is present in the composition in a total amino acid amount sufficient to maintain total protein aggregation at less than 5% following exposure of the composition to a temperature for a period of time.

11. The composition of claim 10, wherein the temperature is 25 °C, wherein the period of time is 6 months.

12. The composition of claim 10, wherein the temperature is 5 °C, wherein the period of time is 6 months.

13. The composition of claim 12, wherein the at least one amino acid is present in the composition in a total amino acid amount sufficient to maintain total protein aggregation at less than 2% following exposure of the composition to the temperature for the period of time.

14. The composition of claim 10, wherein the pH of the composition is 6.3 to 7.4.

15. The composition of claim 10, wherein the pH of the composition is 6.7 to 7.1.

16. The composition of claim 1, wherein the composition is in lyophilized form.

17. A kit comprising the composition of claim 1 as a pharmaceutical composition suitable for intravenous administration.