MICROPARTICLES COMPRISING A SULPHUR-CONTAINING COMPOUND

Field of the Invention

The present invention relates to microparticles comprising a sulphur-containing compound, such as cysteamine or cystamine, or a pharmaceutically acceptable salt, hydrate or ester thereof.

Background to the Invention

Cystic fibrosis (CF) is a multisystem disorder caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene, located on chromosome.

Lung disease remains the leading cause of morbidity and mortality in patients with CF [Davis PB, Drumm M, Konstan MW. Cystic fibrosis. Am J Respir Crit Care Med 1996; 154:1229; Goss CH, Rosenfeld M. Update on cystic fibrosis epidemiology; Curr Opin Pulm Med 2004; 10:510; Brennan AL, Geddes DM. Cystic fibrosis. Curr Opin Infect Dis 2002; 15:175; Gibson RL, Burns JL, Ramsey BW. Pathophysiology and management of pulmonary infections in cystic fibrosis. Am J Respir Crit Care Med 2003; 168:918.

One of the major drivers of CF lung disease is infection (Sagel SD, Gibson RL, Emerson J, et al. Impact of Pseudomonas and Staphylococcus infection on inflammation and clinical status in young children with cystic fibrosis. J Pediatr 2009; 154:183; Cystic Fibrosis Foundation Annual Patient Registry 2013. Available at: http://www.cff.org/research/ClinicalResearch/PatientRegistryReport/ (Accessed on August 07, 2015).

The approach to treating infection in CF is multifaceted, involving antibiotics, chest physiotherapy, inhaled medications to promote secretion clearance, and anti-inflammatory agents. Undoubtedly, improved use of antibiotics is responsible for a substantial portion of the increased survival that has occurred in patients with CF (Brennan AL, Geddes DM. Cystic fibrosis. Curr Opin Infect Dis 2002; 15:175; Sagel SD, Gibson RL, Emerson J, et al. Impact of Pseudomonas and Staphylococcus infection on inflammation and clinical status in young children with cystic fibrosis. J Pediatr 2009; 154:183).

There remains a need for better therapies for treating and preventing lung diseases/conditions in particular those associated with mucous-rich environments such as the CF lung. In addition there remains a need to limit the amount or doses of antibiotics used with the introduction of novel, replacement therapies or adjunct treatments that can improve the effectiveness of currently available treatments in the treatment or prevention of bacterial infections, in particular in the CF lung.

Surprisingly, we have shown that microparticles provide a useful mode of delivery for cysteamine to patients with lung disease.

Summary

In one aspect, the present invention provides for microparticles comprising cysteamine, cystamine or a pharmaceutically acceptable salt, hydrate or ester thereof, and a stabilizing agent wherein the stabilizing agent is selected from the group consisting of:

monosaccharides, disaccharides, trisaccharides, oligosaccharides and corresponding sugar alcohols, polysaccharides and chemically modified carbohydrates wherein the microparticles have a particle size of 1 to 8 microns.

In another aspect, the present invention provides for a use of microparticles as disclosed herein in the manufacture of a medicament for treating or preventing a lung disease.

In yet another aspect, the present invention provides for a therapeutic composition comprising microparticles as disclosed herein, and at least one additional pharmaceutical agent.

In yet another aspect, the present invention provides for an inhalation device comprising microparticles or a composition as disclosed herein.

Statements of the Invention

According to a first aspect of the present invention there is provided a microparticle or microparticles comprising a sulphur-containing compound, or a pharmaceutically acceptable salt, hydrate or ester thereof.

Claims:

1. Microparticles comprising cysteamine, cystamine or a pharmaceutically acceptable salt, hydrate or ester thereof, and a stabilizing agent wherein the stabilizing agent is selected from the group consisting of: monosaccharides, disaccharides, trisaccharides, oligosaccharides and corresponding sugar alcohols, polysaccharides and chemically modified carbohydrates wherein the microparticles have a particle size of 1 to 8 microns.

2. Microparticles as claimed in any one preceding claim wherein the particles have a particle size of about 4 to 8 microns or 2 to 4 microns or 1 to 4 microns.

3. Microparticles as claimed in any one preceding claim, wherein the pharmaceutically acceptable salt is cysteamine bitartrate.

4. The microparticles as claimed in any one preceding claim wherein the stabilizing agent is trehalose, or a sugar alcohol such as mannitol.

5. The microparticles as claimed in any preceding claim which comprises up to 20%w/w cysteamine, cystamine or or a pharmaceutically acceptable salt, hydrate or ester thereof.

6. The microparticles as claimed in claim 5 which comprises between about 5 and 10% w/w cysteamine, cystamine or a pharmaceutically acceptable salt, hydrate or ester thereof.

7. The microparticles as claimed in any preceding claim which comprises up to 85% stabilising agent.

8. The microparticles as claimed in any preceding claim which comprises between: a) 70 and 95% w/w; or b) 80 and 95% w/w stabilizing agent.

9. The microparticles as claimed in any preceding claim which further comprises leucine.

10. The microparticles as claimed in claim 9 which comprises between 1 and 10% leucine.

11. Use of microparticles as claimed in any one of claims 1 to 10, in the manufacture of a medicament for treating or preventing a lung disease.

12. The use of claim 11, wherein the lung disease is a respiratory disease.

13. The use of claim 11, wherein the lung disease is cystic fibrosis, chronic obstructive pulmonary disease, chronic bronchitis, bronchiectasis, emphysema, chronic obstructive airways disease, chronic cough, common cold, influenza, hantavirus, pneumonia or pleurisy.

14. A therapeutic composition comprising microparticles as claimed in any one of claims 1 to 10, and at least one additional pharmaceutical agent.

15. The therapeutic composition as claimed in claim 14 wherein the additional pharmaceutical agent is an antibacterial agent; optionally wherein the additional pharmaceutical agent is selected from the group consisting of antibiotics, mucolytic agents, vasodilators such as bronchodilators, antihypertensive agents, cardiovascular drugs and calcium channel blockers.

16. An inhalation device comprising microparticles as claimed in any one of claims 1 to 104, or a composition as claimed in any one of claims 14 to 15.