Pulmospheres – a novel pulmonary drug delivery system

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Abstract
Pulmospheres represent a novel breakthrough in particle engineering. The hollow/porous design, excellent stability of these homodispersions in HFA (ozone friendly propellant) suspensions, aerodynamic properties, and other attributes are expected to allow for use of Pulmospheres to deliver a variety of drug substances via metered-dose inhalers, dry powder inhalers, nebulizers, and other devices.

The development of an inhalant therapy that is efficacious and safe depends not only on a pharmacologically active molecule, but also on a well-designed delivery system and formulation. It is the optimization of the whole system (drug, drug formulation and device) that is necessary for the successful development of inhalation therapies, both new and old, for the treatment of local and systemic diseases. Drug–device combinations must aerosolize the drug in the appropriate particle size distribution and concentration to ensure optimal deposition and dose in the desired region of the lung.

The lung has served as a route of drug administration for thousands of years. The origin of inhaled therapies can be traced back 4000 years ago to India, where people smoked the leaves of the Atropa belladonna plant to suppress cough. In the 19th and early 20th centuries, asthmatics smoked asthma cigarettes that contained stramonium powder mixed with tobacco to treat the symptoms of their disease.

Keywords: Pulmospheres, applications
The surface area of human adult lungs is similar to that of a small apartment, between 550 and 1,100 square feet. The primary role of the lung is the exchange of oxygen and carbon dioxide. Gas exchange occurs in the roughly 300 million alveoli, which are spherical outcroppings at the end of approximately 20 branches of conducting airways. The lungs provide the most direct route of entry for medications into the bloodstream. Once in the bloodstream, medications gain access to all parts of the body including the brain. For psychoactive substances such as nicotine, pulmonary delivery has long been recognized as the most efficient route of delivery. Pulmonary drug delivery has been limited to this point, due to an absence of technology that allows this route to be utilized.

PulmoSpheres represent a novel breakthrough in particle engineering. The hollow/porous design, excellent stability of these homodispersions in HFA (ozone friendly propellant) suspensions, aerodynamic properties, and other attributes are expected to allow for use of PulmoSpheres to deliver a variety of drug substances via metered-dose inhalers, dry powder inhalers, nebulizers, and other devices.

PulmoSpheres create a “smoky”, homogeneous plume when administered via dry powder is a culmination of expertise with fluorochemicals, surfactants, emulsions, and spray-dried powders. PulmoSpheres are produced by mixing a drug and a surfactant to form an emulsion which is spray-dried into microscopic spheres that can be suspended in a fluorochemical propellant or carrier for delivery of medications into the lungs or nasal passages powder inhalers. This may indicate that less drug loss due to precipitation out of the plume compared to other drug formulations. PulmoSpheres have been formulated with a variety of medicaments, including asthma drugs, non-steroidal and steroidal anti-inflammatory drugs, antibiotics, proteins and peptides, and other drug substances.

Inhalation Market

According to the latest World Health Organization estimates (2007), currently 300 million people suffer from asthma and 210 million suffer from chronic obstructive pulmonary disorder - COPD. Asthma is the most common chronic disease among children and the leading cause of hospitalization. The prevalence of asthma increased 75% from 1980-1994; asthma rates in children under age five increased more than 160% during that time period. Three million people died from COPD in 2005. Fatalities are projected to increase by more than 30% in the next ten years. The disease is poised to become the third leading cause of death worldwide by 2020.
The value of the inhaled drug market has been estimated at $18.5 billion globally for 2006. As can be seen from the chart below, asthma and COPD represent the largest market segment, 65%, of the inhaled drug market worldwide. The chart also illustrates the many market opportunities for inhaled drugs. The world market for asthma drugs is expected to exceed $21.94 billion by 2010 with the US market accounting for approximately half of the global total.

In terms of revenue, the asthma and COPD therapeutics area historically ranks as the 6th largest single source of sales revenue for the pharmaceutical industry. The entire respiratory market is the 4th largest therapeutic area by sales and generated nearly $32.4 billion globally in 2005. Sales have grown steadily in the US and account for approximately 54% of global respiratory sales. The rise in the incidences of asthma and COPD combined with the possibilities of delivering many other medications through inhalation create a significant market opportunity. In addition, as pipelines weaken and many blockbuster drugs are coming off patent, the pharmaceutical companies are scrambling for new sources of revenue.

**Advantages of Pulmosphere**

The poor powder dispersibility found with current dry powder inhaler (DPI) and pulmonary metered dose inhaler (pMDI) formulation of micronized drug can be overcome through use of pulmosphere technology.
Problems associated with the MDI formulation are

- Clogging
- Agglomeration
- Caking
- Particle size growth

A Pulmosphere is more efficacious due to:

- Faster onset of action
- Higher bioavailability rate
- Freedom from injections
- Less side effects

Drug Candidates for Future Biotech Inhalers

Insulin, Growth factors (local & systemic), Interferon’s, Lung surfactants, Monoclonal antibodies, Receptors, Viral vectors

As more efficient pulmonary delivery devices and sophisticated formulations become available, physicians and health professions will have a choice of a wide variety of device and formulation combinations that will target specific cells or regions of the lung, avoid the lung’s clearance mechanisms and be retained within the lung for longer periods. The more efficient, user-friendly delivery devices may allow for smaller total deliverable doses, decrease unwanted side-effects and increase clinical effectiveness and patient compliance.