A New Era for Mesh Nebulisers

Mesh nebulisers in conjunction with innovative treatments are creating a new era of drug-device combination products that aim to target all types of respiratory diseases

Hernan Cuevas Brun at HCmed Innovations

Nebulisers have been an important device for inhalation therapy since their invention in the 19th century. Throughout the years, different technologies have been developed with the goal of further improving the treatment of respiratory diseases. Today, new devices offer the possibility to generate innovative approaches, overcoming previous limitations and widening the use of nebulisers in areas that have not been explored yet.

The Evolution of Nebulisers

To depict a clearer picture of the evolution of nebulisers, it is essential to start with the invention of the jet nebulisers, which resulted in a massive breakthrough when they were first introduced as a medical device in the respiratory field. This event constituted itself as a pillar that opened a new chapter in the history of inhalation therapy and still has vast implications nowadays.

About a century later, in the mid-20th, the ultrasonic nebulisers were introduced with their new features and advantages. The objective of developing this new device was to improve nebulisation experience. However, it was not until the appearance of mesh nebulisers, at the end of the 20th century, that a revolution among nebulisers occurred, catching the attention of professionals in the medical field thanks to the higher levels of efficiency of these devices. Moreover, mesh nebulisers have been proven to broaden the areas of application when compared to their predecessors.

Respirable Fraction and Aerosol Characteristics

When it comes to the treatment of respiratory diseases such as chronic obstructive pulmonary disease (COPD) and cystic fibrosis, particles reaching the respirable fraction are indispensable to achieve effective treatment. The respirable fraction is defined as the mass fraction of aerosol that counts with droplets that have between 1 and 5µm in diameter. The size of these particles is defined as being small enough to go through the airways and reach the alveoli in the lungs. This is an

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essential requirement to treat many medical conditions affecting the respiratory system.

The characteristics of aerosol particles produced during nebulisation are represented by a set of parameters that provide basic information about the nebulised medication. Perhaps the most spoken term is the mass median aerodynamic diameter that refers to the particle size distribution of aerosol. Two other important parameters are the fine particle dose (FPD) and fine particle fraction (FPF), both of which account for the aerosol fraction that is below 5µm in diameter in accordance to the definition of respirable fraction. While the FPF refers to the percentage of the total output with particles below 5µm in diameter, the FPD describes the amount of drug comprised in that same fraction based on the amount of the drug being nebulised. Additionally, the output rate and delivered dose reveal about the rate at which the medication is aerosolised and the total dose being delivered during nebulisation, respectively.

There are various methods that can be used to measure the parameters described above. However, both the US and European Pharmacopeia encourage the use of the Next Generation Impactor to calculate the aerodynamic particle size distribution. Although laser particle sizers can also be used for the same purpose, and they are easier to operate, their accuracy is still questioned by some specialists in the field. High-performance liquid chromatography and ultraviolet spectrophotometers can also be used to analyse particle size, and in some cases, are utilised in conjunction with breathing simulators to analyse a larger number of parameters.

Mesh Technology

Mesh technology was first developed in the 1990s. It is described as a mechanism that consists of a mesh membrane in direct contact with the liquid to be aerosolised. The mesh membrane in the nebuliser oscillates due to an ultrasonic vibration that is driven by a piezoelectric component, allowing the transformation of fluids into aerosol containing tiny droplets that can be inhaled deeply into the lungs under the proper conditions.

Based on their structure, mesh nebulisers can be classified into two categories: passive and active. The vibration of the mesh in passive mesh nebulisers is driven by a horn piezo component that oscillates producing fine particles when the liquid goes through the mesh; similarly, the active nebulisers generate the same results, but in their case, the piezo component is directly attached to a plate that contains both the mesh membrane and the piezo component.

Mesh nebulisers have definitely initiated a new era for the nebuliser industry. They are not only portable and quieter, but also provide higher performance in many aspects when compared to their predecessors. A large number of studies have so far demonstrated that mesh technology is able to deliver higher doses of medication in shorter time with much lower waste or residues. In recent years, the interest of pharmaceutical companies to conduct clinical studies on mesh nebulisers has increased steadily, and this trend is expected to remain as the nebulisation field continues to evolve.

Unfortunately, besides the improvements offered by mesh nebulisers, their penetration in the market is still debatable three decades after their introduction in the market. Higher cost is probably the biggest issue for the end consumer. Therefore, market diversification may be one of the most favourable approaches at this point as consumers become more aware of the characteristics and benefits of mesh technology.

Drug-Device Combination

As the medical field continues to develop, the idea of combining medications and devices is becoming more appealing to pharma companies. Regulations vary along territories; nonetheless, in countries and regions where regulations about combination products are in place, pharma companies are aiming for the

treatment of new indications. This slightly recent concept has already seen several products launched in the respiratory market. However, what is the reason behind this concept? Perhaps the main explanation is the desire to optimise drug delivery. Pharma companies and companies working with mesh technology are partnering in order to create combination products that can increase drug delivery and reduce waste of expensive formulations. The main purpose of these partnerships lies on the customisation of the mesh nebuliser to fulfill the requirements of the formulation to be nebulised, thus achieving a more effective treatment. This approach intends to generate a new wave of products that will be based on tailoring devices to enhance drug delivery for inhalation therapy.

The flexibility of innovative mesh nebulisers is certainly set to play an important role in the years to come. It should not be surprising that the number of new indications to be targeted could also increase as the technology is refined and there is more information about rare diseases. Companies around the world may expect the opening of new possibilities regarding these points in the next few years.

Potential Challenges to Overcome

Although there are many benefits that could come along with the implementation of more drug-device combination products, there are also certain challenges that partnerships may have to overcome as these collaborations are forged and implemented.

Companies may be looking into diverse aspects of this business model, and without a doubt, its profitability may come into question for some professionals in the field. As combination products are characterised by higher costs, more conservative pharma companies may consider not to adopt this approach, but rather go for minimum-risk approaches when it comes to development of new products. Nevertheless, combination products could remain appealing to players who desire to innovate and provide treatment for diseases that are not receiving enough coverage at this point, or in other cases, there could be pharma companies that would like to improve existing treatment for well-studied conditions.

Equally, changes in regulation are expected to weigh in as the future of this field is shaped. The expectations are high, and the hopes of professionals to offer more effective treatments are enormous. The 2020s will serve as a canvas to see how the facts unfold to prove the success or failure of new applications driven by mesh technology. This will be an era that aims to focus on the treatment of common respiratory diseases as well as more rare ones such as COPD, primary immunodeficiency disease in the lungs, and pulmonary arterial hypertension. Helping smaller groups of patients who suffer from less common diseases is surely under the radar of many companies around the world.

Hernan Cuevas Brun studied Biomedical Engineering at National Tsing Hua University in Hsinchu, Taiwan, at which he did research focusing on drug delivery for several years. After obtaining an MBA degree, he joined **HCmed Innovations** where he was appointed as Marketing Manager. He has helped rebrand the mesh nebuliser manufactured by HCmed, which is based on a drug-device combination platform to enhance inhaled drug delivery. Besides working on the marketing strategy of the company, Hernan also collaborates in the participation arrangements of HCmed in four major conferences every year: the Drug Delivery to the Lungs Conference, the European Respiratory Society International Congress, the Respiratory Drug Delivery Conference, and the American Thoracic Society Conference.

henry@hcmed-inno.com