



AN INTRODUCTION TO SMART BREATH-ACTUATED NEBULISERS

In this article, Edgar Hernan Cuevas Brun, Marketing Manager at HCmed Innovations, considers the benefits of smart breath-actuated nebulisers and looks at the latest technology contributing to the evolution of nebulisers.

THE ROLE OF NEBULISERS IN INHALATION THERAPY

Inhalation therapy has been proven to provide a more direct and effective treatment for diseases that affect the respiratory system. The active action of inhaled medication used to treat illnesses affecting the respiratory tracts is supported by a lower dose requirement that translates into higher effectiveness and lower incidence of systematic adverse effects.¹

Among the devices commonly used in inhalation therapy, nebulisers have long occupied an essential spot. The first nebulisers date back to the 1800s.² Transitioning from larger jet nebulisers requiring the use of loud compressors, to more recent portable and silent mesh nebulisers that aerosolise liquid medication by relying on ultrasonic frequencies that vibrate a mesh membrane, nebulisers, have established themselves as a top instrument to deliver inhaled medication, especially when it comes to population groups that may struggle with the use of dry powder inhalers (DPIs) and metered dose inhalers (MDIs).³

As is well documented, the use of MDIs and DPIs requires either good co-ordination to successfully deliver medication into the lungs, or high inspiratory flow, both of which can cause the mishandling of these devices, leading to lower therapeutic efficacy. Therefore, the two major groups that greatly benefit from the use of nebulisers are children under the age of five and the elderly. Nebulisers can be a good solution for patients with certain

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conditions that prevent them inhaling their medication properly with other devices. Some medications that are administered in the form of inhaled drugs include corticosteroids, bronchodilators such as muscarinic antagonist and beta agonists, antibiotics and more recent innovative biologic drugs.³

THE BENEFITS OF BREATH-ACTUATED NEBULISERS

Breath actuation is a feature of nebulisers that has attracted plenty of attention in recent years, particularly when it comes to the development of new inhalation devices. In order to improve drug delivery, the incorporation of a mechanism or sensor that triggers aerosol generation during inhalation provides several benefits.⁴ One example is the amount of drug released into the environment when users exhale becomes minimal. This is highly favourable when delivering costly APIs.

Although the number of breath-actuated nebulisers is comparatively small when



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analysing the entire group of commercially available devices, evidence of the benefits of breath-actuated devices has increased in the last decade. In some cases, findings suggest that, in addition to the benefits of the delivered dose from breath-activated devices, aerodynamic particle size distribution also remains within the respirable range (2-5 µm), a condition that is fundamental for better lung deposition.^{4,5} Consequently, smaller amounts of APIs are required for the treatment with these nebulisers.

A drawback of this technology is that, as the drug is not continuously aerosolised, nebulisation time can be compromised, resulting in extended periods of time to complete treatment.⁶ Nonetheless, this can be offset by lower volumes required to reach the same nominal dose.

BREATH ACTUATION EFFECTIVELY REDUCES FUGITIVE AEROSOL

In some instances, the use of nebulisers has been undermined due to the existence of fugitive aerosols. Fugitive aerosols refer to inhaled aerosols that do not deposit in the respiratory tract and are exhaled during exhalation. Aerosol released directly into the environment during the exhalation period of continuous nebulisation is also known as a fugitive aerosol. Both of these definitions have been reported to be hazardous to people around the individuals receiving treatment, as particles can remain airborne for times ranging from a few minutes to a number of hours.⁶

Previous studies have demonstrated that medical professionals and caregivers who assist patients during their inhalation treatment are exposed to inhaling unnecessary medication, which can potentially produce toxic side effects. Such is the incidence that more than 45% of the nominal dose could end up as a second-hand medical aerosol under continuous nebulisation.⁷ Moreover, constant

inhalation of antibiotics could also lead to the development of antimicrobial resistance.

There is also speculation about the possibility of spreading diseases through the inhaled aerosol that is exhaled when droplets are not properly deposited in the lungs. Although the evidence supporting this claim has not been extensively covered in the literature, several institutes and organisations have advised against the use of nebulisers when patients have to be treated for highly infectious diseases, such as in the case of this year's covid-19 pandemic, to avoid the spreading of the virus.⁸

As a solution, the introduction of breath-actuated nebulisers substantially reduces the emission of these fugitive aerosols, decreasing the amount of API being wasted in the environment and providing a safer surrounding for those who share the space with people receiving inhalation treatment.

THE DAWN OF SMART NEBULISERS

In the past decade, the Internet of Things (IoT) has also begun to penetrate the medical field. Nowadays, the better known Medical IoT describes the principal of using connectivity to create a new network that connects medical professionals, patients and caregivers, aiming to share data in real time of a patient's course of treatment.⁹ According to some specialists, its implementation could eventually become the new standard for medical practice.

Patient adherence has long been a concern in the treatment of diseases, including respiratory conditions such as asthma and chronic obstructive pulmonary disease (COPD). In the case of these and other diseases, patients are required to follow doctors' instructions accurately to keep their symptoms under control. Before the introduction of smart nebulisers, physicians had to rely on the subjective information provided by patients that may have not always been entirely accurate.⁹ However, in the new era of smart nebulisers, it is possible to record treatment information and generate logs or reports so

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that medical practitioners can assess the status of patients and decide on future steps for a more suitable line of treatment.¹⁰

The development of cloud platforms also allows the safe storage of private information, compiling clinical history that can be readily stored and displayed. Furthermore, smart nebulisers can assist in enhancing patient adherence by allowing the set-up of alarms, reminders and the display of educational material. Several research studies have reported that the features of smart inhalers can help to enhance patient compliance.¹¹

All of the previously described functions are expected to continue evolving thanks to the advancements in wireless connectivity. This is also the case with mobile applications that transmit information via Bluetooth connectivity, which is currently the main platform to connect inhalation devices to medical clouds through mobile devices.

ADVANCEMENTS IN PATIENT COMPLIANCE

The establishment of new treatment options with innovative biological approaches may require tightening up the development of combination products to optimise treatment. New clinical trials have been focusing on mesh technology as the main source for the development of new drug-device products. The selection of mesh nebulisers over jet and ultrasonic nebulisers is supported by the fact that the former products are portable, silent and more suitable to deliver different types of medication than their counterparts.¹²

Launched nearly three decades ago, mesh nebulisers have various advantages. Therefore, several companies have created platforms that allow the customisation of their devices for specific drugs as combination products.^{13,14} This is indispensable as the final goal is to optimise drug delivery by linking a specific device with a corresponding drug. Since each

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formulation has different characteristics, this drug-device combination system could only achieve optimal results as a pair.¹⁵

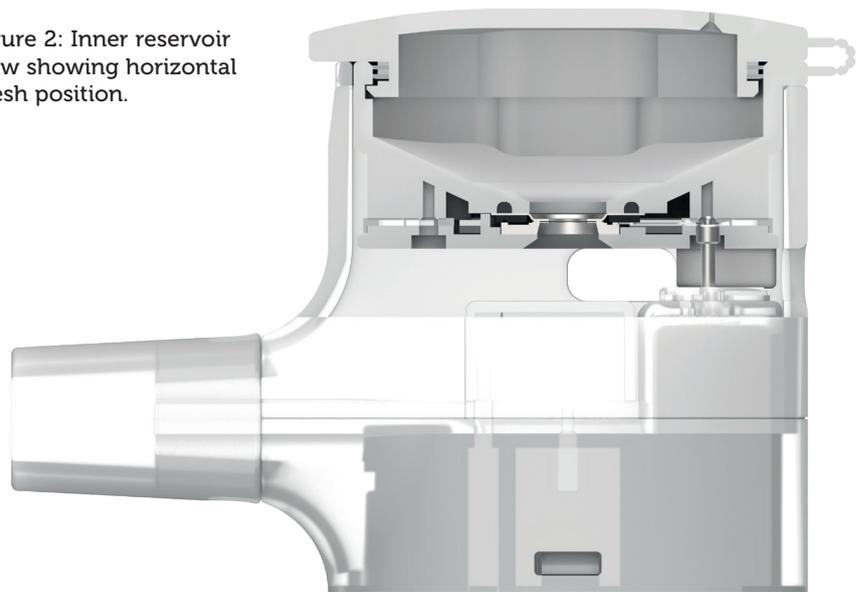
Aiming to strengthen compliance and support drug-device combination development, the application of Bluetooth connectivity and near field communication (NFC) technology can add the function to link the usage of nebulisers and specific drugs as an activating mechanism so that the combination product can be used safely. By doing so, the main objective of enhancing compliance can be further reinforced.

COMBINING THE LATEST INNOVATIONS

The development of new devices targets the incorporation of most of the functions described in the previous sections with the purpose of improving patient adherence, while offering an optimised treatment. It is fundamental for innovative devices to deliver solutions to the market needs, improving treatment conditions and efficiency.

The AdheResp breath-actuated mesh nebuliser, developed by HCmed

Figure 2: Inner reservoir view showing horizontal mesh position.



Innovations, is a new device that combines breath actuation and connectivity features (Figure 1). In this device, the breath actuation is supported by the incorporation of a pressure sensor that enables the detection of pressure variation, which occurs during inhalation. This variation activates the aerosol generating structure, converting liquid medication into mist.

One of the main advantages of this mechanism is that fugitive aerosol becomes virtually negligible as the software enclosed in the device is configured to deliver aerosol within an optimal time range.

Bluetooth connectivity is another indispensable tool for smart devices that is part of AdheResp. By allowing the transmission of information from the device to a mobile application, a secure network to store data in the cloud is under development to monitor and solidify patient compliance through a user-friendly interface. Moreover, adherence is also enriched by the addition of NFC technology that binds the drug to the device in a combined system that optimises drug delivery. The optimised product is the result of an extensive and comprehensive development process, which originated from research studies from HCmed, and has matured throughout collaborations established with pharmaceutical companies.

Another additional characteristic of the AdheResp device is that the mesh membrane has been strategically placed in a

horizontal position to minimise residual volume, thus becoming an ideal platform for the delivery of high therapeutic drugs (Figure 2). The chamber structure of the device also contributes to the airflow and delivery of medication, operating with the patented mesh technology of HCmed that supports nebulisation of a wide range of medications that include most recent biologic formulations. The aerosol particle size distribution parameters can further be controlled



Figure 1: AdheResp breath-actuated mesh nebuliser.



Figure 3: Front LED-light panel displaying power, Bluetooth and battery status icons.



Figure 4: USB Type-C port at the back of AdheResp.

according to the nature of each formulation, ensuring optimal lung deposition.

To complete a well-rounded device, the usability of AdheResp was closely examined to present a slick and intuitive design that allows patients from all ages to manoeuvre through the functions of the mesh nebuliser (Figure 3). This device can be easily disassembled to be properly cleaned and disinfected, safeguarding

the well-being and comfort of patients. Moreover, it comes with a Type-C USB port to facility charging (Figure 4).

CONCLUSION

The incorporation of a new series of smart advancements is creating distinctive applications and differentiating devices in the respiratory field. The integration of

new solutions is expected to satisfy an increasingly growing market that demands more effective, simple, connected and affordable options for inhalation devices in order to contribute to the evolution of nebulisers.

This new era, more than ever, requires the collaboration of pharmaceutical companies, device developers, physicians and patients to address an expanding population that has been seriously affected by respiratory diseases due to pollution, overpopulation and other factors.

Smart breath-actuated mesh nebulisers, such as AdheResp, merge features that could drive further development of inhalation therapy, and that could create a completely new treatment experience in the worldwide fight against diseases. As the development of this type of device continues to flourish, the contribution of each player is indispensable to deliver more effective treatment solutions for patients who require their daily inhalation treatment.

ABOUT THE COMPANY

HCmed Innovations is focused on the development of drug-device combination products for inhalation therapy. It develops and manufactures portable vibrating mesh nebulisers that offer a mature customisation platform. This technology enables efficient and reliable nebulisation of different types of medication, including small molecule synthetics and large molecule biologics, as either solutions, suspensions or even difficult-to-deliver high viscosity drugs. The newest products include the incorporation

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of breath actuation and connectivity features to enhance drug delivery and reinforce patient adherence.

REFERENCES

1. Salvi S, Gogtay J, Aggarwal B, "Use of breath-actuated inhalers in patients with asthma and COPD - an advance in inhalational therapy: a systematic review". *Expert Rev Respir Med*, 2014, Vol 8(1), pp 89–99.
2. Sorino C et al, "Inhalation therapy devices for the treatment of obstructive lung diseases: the history of inhalers towards the ideal inhaler". *Eur J Intern Med*, 2020, Vol 75, pp 15–18.
3. Kesten S et al, "Development of a novel digital breath-activated inhaler: Initial particle size characterization and clinical testing". *Pulm Pharmacol Ther*, 2018, Vol 53, pp 27–32.
4. Ari A, Fink JB, "Breath-actuated nebuliser versus small-volume nebuliser: efficacy, safety, and satisfaction". *Respir Care*, 2012, Vol 57(8), pp 1351–1353.
5. Sabato K et al, "Randomized controlled trial of a breath-actuated nebuliser in pediatric asthma patients in the emergency department". *Respir Care*, 2011, Vol 56(6), pp 761–770.
6. McGrath JA et al, "Investigation of the Quantity of Exhaled Aerosols Released into the Environment during Nebulisation". *Pharmaceutics*, 2019, Vol 11(2), p 75.
7. Ari A, Fink JB, Pilbeam SP, "Secondhand aerosol exposure during mechanical ventilation with and without expiratory filters: An in vitro study". *Ind J Resp Care*, 2016, Vol 5, pp 677–682.
8. Fink JB et al, "Reducing aerosol-related risk of transmission in the era of covid-19: An interim guidance endorsed by the International Society of Aerosols in Medicine". *J Aerosol Med Pulm Drug Deliv*, 2020, Vol 12. Epub ahead of print.
9. Chen J et al, "The effect of electronic monitoring combined with weekly feedback and reminders on adherence to inhaled corticosteroids in infants and younger children with asthma: a randomized controlled trial". *Allergy Asthma Clin Immunol*, 2020, Vol 16, 68, e-collection 2020.
10. Daniels T et al, "Accurate assessment of adherence: self-report and clinician report vs electronic monitoring of nebulisers". *Chest*, 2011, Vol 140(2), pp 425–432.
11. Chan AH et al, "Adherence monitoring and e-health: How clinicians and researchers can use technology to promote inhaler adherence for asthma". *J Allergy Clin Immunol Pract*, 2013, Vol 1(5), pp 446–54.
12. Pritchard JN et al, "Mesh nebulisers have become the first choice for new nebulized pharmaceutical drug developments". *Ther Deliv*, 2018, Vol 9(2), pp 121–136.
13. Gessler T, "Iloprost delivered via the BREELIBTM nebuliser: a review of the clinical evidence for efficacy and safety". *Ther Adv Respir Dis*, 2019, Vol 13, DOI: 10.1177/1753466619835497.
14. Kerwin E, Ferguson GT, "An overview of glycopyrrolate/eFlow® CS in COPD". *Expert Rev Respir Med*, 2018, Vol 12(6), pp 447–459.
15. Dhand R, "Intelligent nebulisers in the age of the Internet: The I-neb Adaptive Aerosol Delivery (AAD) system". *J Aerosol Med Pulm Drug Deliv*, 2010, Vol 23, Suppl 1(Suppl 1):iii-v.

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Edgar Hernan Cuevas Brun, Marketing Manager at HCmed Innovations, is responsible for the marketing analysis and research of new products as well as the branding of HCmed’s commercially available mesh nebulisers. He has more than five years of experience in the drug delivery field, holding a degree in biomedical engineering and an MBA. He is also in charge of co-ordinating HCmed’s participation and publications in major conferences, such as the European Respiratory Society International Congress and the American Thoracic Society Conference.

HCmed Innovations is a trusted and efficient partner for the development of drug-nebuliser combination products.

Newly integrated features



BREATH ACTUATION



LOCK AND KEY SYSTEM



CONNECTIVITY AND IOT



For more information about our mesh nebulisers and APSD analysis services visit our website www.hcmed-inno.com or email us to info@hcmed-inno.com

