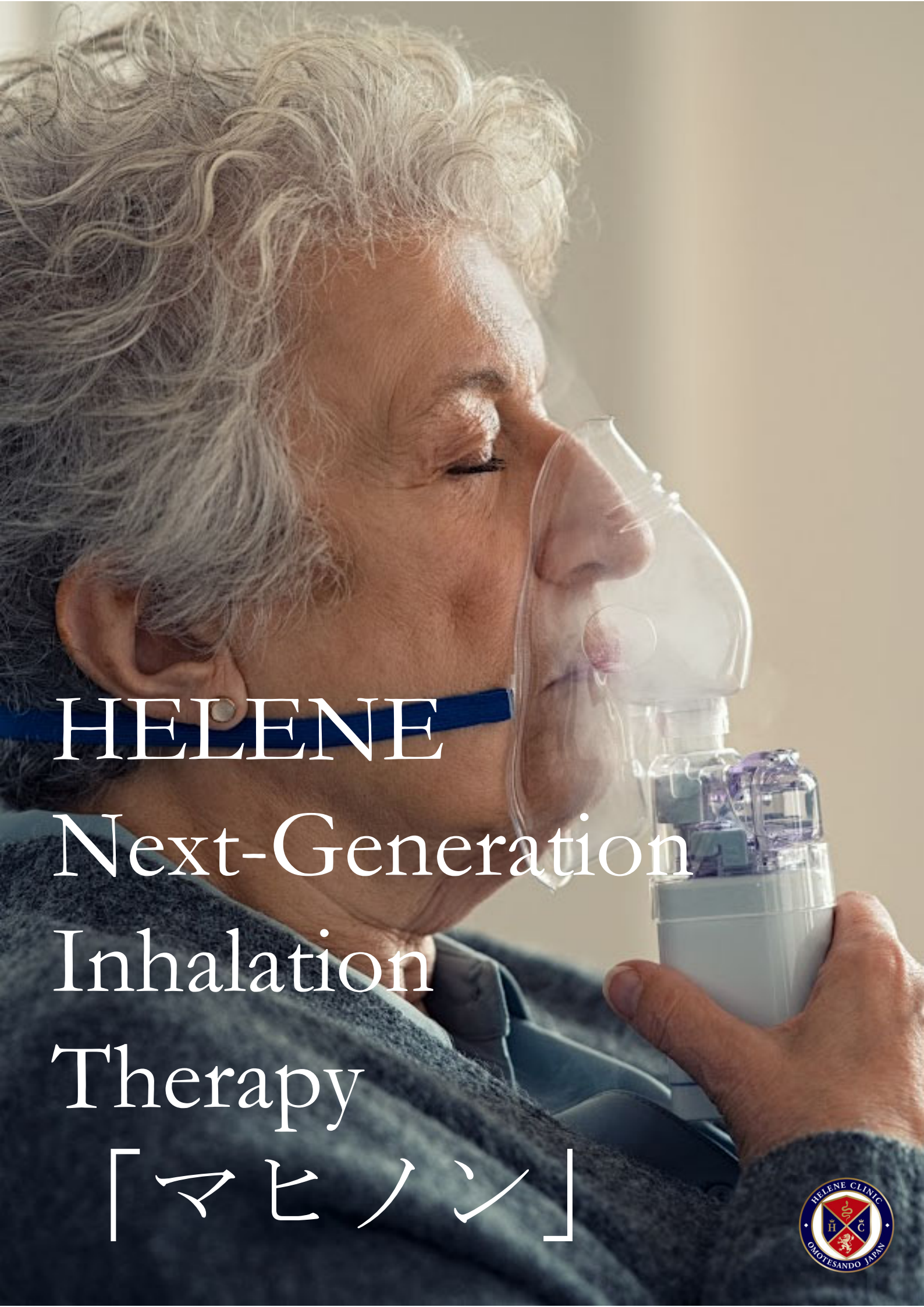
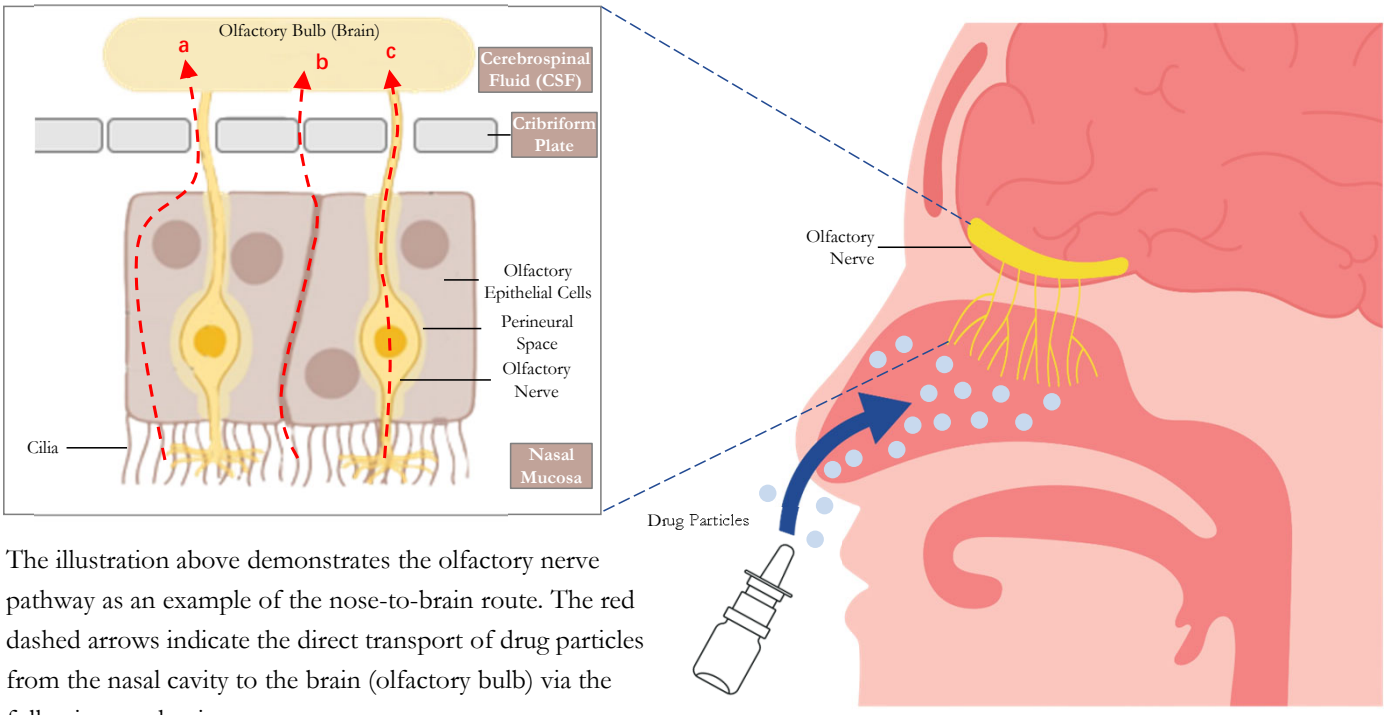


HELENE Next-Generation Inhalation Therapy 「マヒノン」

HOW THE DRUG REACHES THE BRAIN: THE NOSE-TO-BRAIN PATHWAY

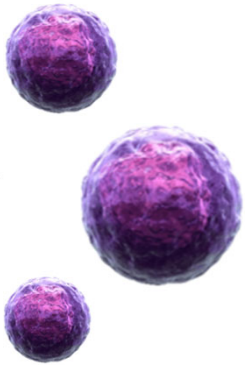
The nose-to-brain pathway is a non-invasive drug delivery route through which medications are administered via the upper nasal cavity—particularly the olfactory region—directly into the central nervous system (CNS). Drugs can reach the brain either through the olfactory and trigeminal nerves or by diffusing through the intercellular matrix into the cerebrospinal fluid (CSF), thereby bypassing the blood-brain barrier (BBB), which often limits the efficacy of traditional oral or intravenous delivery methods. In addition, the nasal cavity is highly vascularized and richly innervated, enabling rapid transport of therapeutic agents to targeted brain regions.



The illustration above demonstrates the olfactory nerve pathway as an example of the nose-to-brain route. The red dashed arrows indicate the direct transport of drug particles from the nasal cavity to the brain (olfactory bulb) via the following mechanisms:

a. Transcellular transport through olfactory epithelial cells
b. Paracellular transport between olfactory epithelial cells
c. Intra-neuronal transport along the olfactory nerve

THE OPTIMAL SIZE FOR BRAIN DELIVERY: EXOSOMES



In nose-to-brain drug design, particle size is a critical parameter. It directly influences the site of deposition within the nasal cavity and the efficiency of absorption—both of which determine the likelihood of successful delivery to the central nervous system (CNS). The olfactory region, located at the upper part of the nasal cavity, is the key area for brain entry. If the particle size is too large, it may be cleared by nasal mucus; if too small, it may be inhaled into the lungs and enter systemic circulation, thereby reducing the efficiency of CNS targeting.

Against this backdrop, stem cell-derived exosomes have demonstrated significant potential as carriers for nose-to-brain delivery. With particle sizes ranging between 30 and 150 nanometers, exosomes fall within the optimal size range for nasal transport. They can bypass the blood-brain barrier (BBB) via olfactory or trigeminal nerve pathways, enabling direct access to the CNS.

Furthermore, exosomes exhibit excellent biocompatibility and targeting ability. They can carry a variety of bioactive molecules derived from their parent cells—such as miRNAs, mRNAs, and cytokines—which regulate recipient cell functions and exert neuroprotective, anti-inflammatory, and regenerative effects. Collectively, these attributes position exosomes as one of the most promising nasal drug delivery vehicles for the treatment of CNS disorders.

HOW THE DRUG REACHES THE LUNGS: THE INHALATION DELIVERY PATHWAY

In exosome inhalation therapy, a liquid formulation containing stem cell-derived exosomes is aerosolized into fine micro-sized particles and administered via inhalation, allowing the therapeutic agents to reach the alveolar regions of the lungs for localized treatment. Exosomes are naturally occurring nanoparticles with diameters ranging from 30 to 150 nanometers, a size well-suited for deep pulmonary deposition.

Their small size enables effective delivery to the distal areas of the lungs, including the alveoli, where they can penetrate the airway epithelium and be efficiently taken up by target cells. Derived from the human body, exosomes possess low immunogenicity, and their superior biocompatibility and stability make them highly promising vectors in the field of regenerative medicine.

Mechanism of Delivery

Step 1: Nebulization of Exosomes Using an Atomizer

A specialized device is used to nebulize the exosome solution into fine particles, rendering them suitable for deposition in the alveolar regions.

Step 2: Deposition in the Alveolar Region

The inhaled aerosolized particles travel through the respiratory tract and reach the distal regions of the lungs, where they deposit on the epithelial surface of the alveoli. At this site, exosomes interact with the cell membrane, facilitating the transfer of their cargo into target cells.

Step 3: Localized Therapeutic Action

Exosomes exhibit a range of biological functions, including anti-inflammatory effects, immunomodulation, and tissue regeneration. Within pulmonary tissues, exosomes can help suppress inflammation, promote epithelial repair, and inhibit fibrosis. As a result, this localized therapeutic approach holds the potential to achieve enhanced treatment efficacy while minimizing systemic side effects.

Clinical Evidence in Pulmonary Regeneration and COVID-19

Exosome inhalation therapy has demonstrated significant potential in pulmonary repair and regeneration. In the SENTAD COVID-19 study conducted in the United Arab Emirates (UAE), patients who received nebulized autologous stem cell therapy showed marked improvement compared to the control group.

Among a total of 139 participants (69 in the treatment group and 70 in the control group), 20% of patients in the treatment group exhibited significant clinical improvement ($p < 0.0001$), with results confirmed to be statistically significant. These improvements are attributed to the anti-inflammatory effects of stem cells and their ability to promote lung tissue regeneration, reinforcing the therapeutic promise of exosome inhalation therapy for respiratory conditions such as viral pneumonia, chronic obstructive pulmonary disease (COPD), and pulmonary fibrosis.

Notably, two patients in the treatment group demonstrated particularly remarkable outcomes, offering additional clinical evidence supporting the potential of inhaled stem cell-based therapies.

Case 65
A 38-year-old male with mild obesity, admitted with severe COVID-19 (score 7).
Day 1: Extensive bilateral lung consolidations and lower zone opacities.
Day 4 : Improved left lung appearance; mild worsening on the right.
Day 9 : Further improvement with minor residual in the left lung.

Case 70
A 47-year-old overweight male (BMI 27.88), ICU stay for 14 days with severe COVID-19 (score 7) and antibiotic-resistant Staphylococcus epidermidis infection.
Day 1 : Diffuse consolidations in all lung lobes, especially lower zones.
Day 4: Partial improvement on chest X-ray.
Day 13: Persistent but reduced patchy opacities in mid to lower lung zones.

INDEPENDENTLY DEVELOPED BY HELENE: マヒノン

▲ OMRON Nebulizer NE-U200

This product is an inhalation-based therapy in which a liquid formulation containing stem cell-derived exosomes is nebulized into fine aerosols and delivered into the body via the nasal-to-brain pathway. The exosomes are absorbed through the nasal mucosa and can further reach the central nervous system (CNS).

Exosomes contribute to vascular repair, neuromodulation, and suppression of neuroinflammation. Through these mechanisms, this therapy may help improve cerebral blood flow, reduce the risk of cerebral infarction, and is gaining attention as a novel drug delivery strategy for neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease.

In addition, this therapy may also serve as a preventive approach for high-risk individuals. For patients who have already experienced cerebral infarction and exhibit symptoms such as paralysis, the treatment plan will be determined by a physician based on individual clinical evaluation.

How to Use

Use once in the morning and once in the evening, one vial (1 mL) per use.

① Remove the sealing tape from the vial cap and pour the entire contents into the dosing cup.

② Sit upright, position the inhaler at your mouth, press the button, and inhale slowly and deeply.

③ Ensure that the product is refrigerated after each use.

FAQ

Q1. Whose exosomes are used in this product? Is it safe if they are not my own?
We use clinical-grade exosomes derived from established stem cell lines. Exosomes are not cells and exhibit extremely low immunogenicity, making them a legal and safe therapeutic option.

Q2. Is there a risk of carcinogenesis (cancer development)?
Numerous scientific studies have confirmed that mesenchymal stem cells (MSCs) and their exosomes do not induce carcinogenesis.

▲ Video Guide for Use

Q3. Does the MAHINON device require cleaning? How should I clean it?
Yes, the device needs to be cleaned after use. Please refer to the instructional video via the QR code or contact HELENE staff for assistance.

Q4. I added the solution to my MAHINON device, but no aerosol is being produced. What should I do?
Please tilt the device to allow the solution to flow toward the nebulization port. If you continue to experience difficulties, please refer to the video instructions via the QR code or contact HELENE staff for support.

HELENE CLINIC OMOTESANDO JAPAN

Legal Compliance