THE SCIENTIFIC VALIDATION OF NUTRIENT INHALATION

Aerosol Delivery of Nutritional Supplements into the Body

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Background

Inhaled medications have been available for many years for the treatment of lung diseases and are widely accepted as being the optimal route of administration of first-line therapy for asthma and chronic obstructive pulmonary diseases. In recent years, the lung has been studied as a possible route of administration for the treatment of systemic diseases, such as diabetes mellitus. Behind this wave of novel inhalable drugs is the recent development of new inhalation devices that make it possible to deliver larger drug doses (milligram compared with microgram dosing) to the airways and achieve greater deposition efficiency than the older devices (>50% lung deposition vs.≤20% with older devices) . For the lungs to be the target organ or a route of administration, the appropriate amount of agent must be deposited past the oropharyngeal region to achieve therapeutic effectiveness. The site of deposition, that is on central or peripheral airways, and whether the distribution of the inhaled agent is uniform or non-uniform may also play a role in an inhaled agent's effectiveness.

Today, there are more than 65 different inhaled products of more than 20 active ingredients marketed to treat respiratory diseases. Despite the widespread use of inhaled medications, our knowledge is limited regarding the optimal lung deposition, site for local therapeutic response, the factors that determine the absorption, clearance, and the role the bronchial circulation plays in the redistribution of the inhaled agents.

Based on recent studies and advances in medicinal inhalation therapy, this paper proposes to explain and validate those benefits that can also be gained by the inhalation of nutrients into the systemic body as opposed to the traditional oral administration of nutrients.

Advantages of Aerosol Delivery to the Lungs for Systemic Absorption

Inhalation offers many advantages as a route of administration compared with oral, transdermal, nasal or intravenous administration. Recent advances in aerosol and formulation technologies have led to the development of delivery systems that are more efficient and that produce smaller particle aerosols allowing higher doses to be deposited in the alveolar region of the lungs where they are available for systemic absorption.

Advantages of aerosol delivery are:

1. Suitable for a wide range of substances from small molecules to very large proteins.
2. Rapid response.

3. Lungs offer an enormous absorptive surface area (100 m2) and a highly permeable membrane (0.2–0.7 μm thickness) in the alveolar region. Large molecules with very low absorption rates can be absorbed in significant quantities.

4. A less harsh, low enzymatic environment that is devoid of hepatic (liver) first-pass metabolism.

5. Reproducible absorption kinetics.

6. Pulmonary delivery is independent of dietary complications, extracellular enzymes and metabolic differences that affect gastrointestinal absorption.

7. Nutrient Inhalation is a more bioavailable route of administration than ingestion and less invasive than intravenous.

8. Lower dose requirements due to greater absorption of intact nutrients to the bloodstream.

AEROSOL INHALATION AND DELIVERY ABSORPTION FACTORS

Absorption of Small and Large Nutrient Molecules by Inhalation More Efficient Than Ingestion

The lung is the only organ through which the entire cardiac output passes. Before the inhaled nutrient can be absorbed into the blood from the lung periphery, it has several barriers to overcome: lung surfactant, surface lining fluid, epithelium, interstitial and basement membrane, and the endothelium. Nutrient absorption is regulated by a thin alveolar–vascular permeable barrier. The number of alveoli ranges from 200 million to 600 million, resulting in an enormous epithelial surface area with epithelium consisting of a thin single cellular layer (0.2–0.7 μm thickness). While these properties promote efficient gas exchange through passive transport, they also provide a mechanism for efficient nutrient delivery to the bloodstream. It has been hypothesized that large molecules either pass through the cells via absorptive transcytosis (adsorptive or receptor mediated), paracellular transport between bi-junctions or tri-junctions, or through large transitory pores in the epithelium. Thus, the higher bioavailability of macromolecules deposited in the lung (10–200 times greater than nasal and gastrointestinal values) may be due to its enormous surface area, very thin diffusion layer, slow surface clearance and antiprotease defense system.

Nanometer Size Aerosol Particles Easily Enter the Bloodstream

Particles 1–5 μm in diameter are deposited in the small airways and alveoli with >50% of the 3 μm diameter particles being deposited in the alveolar region. In the case of pulmonary agent delivery for systemic absorption, aerosols with a small particle size would be required to ensure peripheral penetration of the agent. Particles <3 μm have an approximately 80% chance of reaching the lower airways with 50–60% being deposited in the alveoli.

Since this is a new area of scientific research, the most effective particle size for the systemic introduction of supplements via the lungs has not been determined. However, the aerosol diameters from nutritional supplement inhalation are an order of magnitude smaller (250 to 450 nanometers) than

the micron size particles used in inhaled medicines, therefore they will more easily reach the alveolar areas of the lung and more easily enter the blood stream.

Nutrient Physical Form and Solubility – Advantage Inhalation

The amount of a nutrient that can be absorbed also depends on its physical form and solubility. Relatively soluble materials (gases or particles) are quickly absorbed into systemic circulation. Absorption through the alveolar membrane is by passive diffusion, following the concentration gradient.

In addition to solubility, the ability to be absorbed depends on the physical form of the agent (that is, whether the agent is a gas/vapor or a particle). The physical form determines the extent of its penetration into the deep lung. As with particle size, the most effective physical form and solubility for the systemic introduction of supplements via the lungs is also being studied by researchers. Again, the advantage goes to inhalation administration due to the larger surface area and lower interference of the lungs compared to alternative methods of administration.

Greater Bioavailability and Lower Dose Required of Nutrients by Inhalation as Compared to Ingestion

The alveolar region has a very large surface area, about 50 times that of the skin. In addition, the alveoli consist of only a single layer of cells with very thin membranes that separate the inhaled air from the blood stream. Oxygen, carbon dioxide, and other gases readily pass through this membrane. Gases and particles, which are water-soluble (and thus blood-soluble), are absorbed more efficiently from the lung alveoli compared to their absorption via the gastrointestinal tract or through the skin. Water-soluble gases and liquid aerosols can pass through the alveolar cell membrane by simple passive diffusion.

The effectiveness of a nutritional supplement is dependent upon its bioavailability; defined as that fraction or percentage of an administered nutritional supplement that becomes available to the target tissue or blood after administration. Nutrients that are traditionally ingested need to go through the gastrointestinal tract where stomach acid, enzymes, dietary complications and metabolic differences create bioavailability problems. It may take many minutes or even hours for nutrients to pass through the GI tract for absorption by the intestines and into the bloodstream. Along the way, ingested nutrients may decompose, react with other body chemicals or be excreted out of the body. This why the nutrient oral dose or serving size can be very large (10 to 100 x more than by inhalation) because many of these nutrients may never reach the bloodstream. Nutrient inhalation shows it to be a more effective means of administration than the standard practice of ingestion because of its greater absorption, quicker response, and lower dose requirements.

Looking Ahead

The inhalation research that has been conducted regarding medicines, proteins and peptides provides a sound scientific basis for applying those findings to the inhalation of vitamins, minerals, and other nutritional supplements. And although there is a scarcity of information on the inhalation of nutrients,

current research studies, like those being conducted by NV Nutrition, are advancing the science of nutrient inhalation.

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Inhaling Medicines: Delivering Drugs to the Body through the Lungs

John S. Patton and Peter R. Byron