The Great Why Questions About Dry Powder Inhalers

The research pertains to the economic burden of asthma and chronic obstructive pulmonary disease and the impact of poor inhalation techniques with commonly prescribed dry powder inhalers as illustrated in three European countries. Currently, the direct cost burden of managing asthma and COPD for people using DPIs is €813 million, €560 million, and €774 million in Spain, Sweden, and the UK, respectively. Poor inhalation techniques comprised 2.2–7.7% of direct costs, totaling €105 million in these three countries alone. When lost productivity costs were included, total expenditure increased to €1.4 billion, €1.7 billion, and €3.3 billion in Spain, Sweden, and the UK, respectively, with €782 million attributable to poor inhalation technique across the three countries.[1,2]

Airflow resistance

A major issue is current airflow resistance: "Current guidance is in the line with these observations, suggesting that passive DPIs are all flow-rate dependent, and that young children and elderly patients are at risk of not being able to achieve the flow rates necessary to effectively disperse the powder. The underlying factors controlling inspiratory pressures, flow rates and dispensing, and dispersion characteristics of the various DPIs explain why this is the case. While it is also clear then that some patients at the extremes of the population, with poor muscle strength, may not be able to achieve the inspiratory flow rates to utilise a given DPI".[3] "In particular, the inspiratory airflow generated by the patient represents the only active force (a passive force for the device) able to produce the micro-dispersion (even if differently sized for each device) of the powdered drug to inhale. On the other hand, the extent of the patient's inspiratory airflow depends on the patient's airway and lung conditions, and, partially, on the intrinsic resistive regimen of the device". "While low resistance DPIs are still regarded as the easiest and the most comfortable devices for the patient, they instead require a high inhalation airflow rate to the patient, not always achievable. The reason is that the role of the other possible force involved in drug deagglomeration".[4]

De-agglomeration

De-agglomeration is a major parameter in DPI design. "Dry powders designed for inhalation are very fine and can easily form agglomeration due to cohesion between individual particles and are hard to aerosolize. Despite the inhaler and formulation designs, patients are required to generate a forceful and deep inhalation through the DPI to de-agglomerate the powder formulation into respirable particles (with an aerodynamic size ≤ 5 μm) for efficient delivery to the lungs".[5]

"In the inhaler, de-agglomeration is one of the most important particle behaviours since it determines the final particle size distribution and hence the FPF. For Capsule-Based DPI, the presence, dimension and movement of the capsule could greatly influence the flow field in the inhaler, as well as the de-agglomeration and dispersion of particles. The capsule is initially placed in the capsule chamber of the DPI and pierced in a certain way before inhalation to allow particles to be fluidised and move out of the capsule. During the inhalation, the high-speed air flow (normally around 60 L/min) from the inlet of the inhaler forces the capsule to rotate and collide frequently with the inhaler wall. This would, for a certain degree, help the de-agglomeration process of the particle clusters and enhance the performance of the DPI. The drug emptying process normally takes about several seconds. It is a rather complex process, involving the interaction of solid capsule, particles and air flow. At an even higher air flow, for example, over 100 L/min, the shattering of the capsule may occur, which will further increase the complexity of the problem".6 Although Capsule DPIs are relatively simple and low-cost device it is absolutely limited their use for patient with high inhaling force over 60L/min which is insufficient for babies, young children, elder people and many lung diseases patients. The result of shaking (rotating) the capsule inside the Capsule DPI still does not guarantee, according to studies, the solution to the agglomeration problem when inhaling into the lungs.

The Great Why Questions

- Why after decades of producing and using DPI's, still the fine particle lung deposition is so low?
- Why is the use of DPI's required complicated, especially for children, babies, the elderly, and those with disabilities?
- Why is the airflow resistance so high in capsule inhalers and is it not suitable for many populations that suffer from breathing problems?
- Why is the high price of inhalers that does not contribute to health in the third world where 3.2 million people die from lung diseases every year?
- Why is it forbidden to exhale into the inhaler and why is it impossible to breathe through the inhaler?
- Why do you need expensive digital inhalers just to cover up the inefficiency of delivering the drug to the lungs?
- Why practically the existing inhalers are not suitable for use for new drugs or biological drugs aiming as lifesaving drugs suffering from the combination of the DPI's inefficiency with the high price of the drug?
- Why is the use of hazardous medical cannabis cigarettes and VAPs still in use?

The answer to all questions is: Engineers, companies, and entrepreneurs are captive to old concepts and they only try to improve them and complicate them in more complex systems to cover the basic performances which do not contribute to users, medical insurance companies, and global health.

As Mr. Jacek Olczak, CEO, of Philip Morris International speech regarding stopping smoking, it's very true for DPI: "It's time to try something else, to try including an innovative approach"

Like years of using polluting vehicles, a new generation of hybrid and electric vehicles is starting!

Hence the revolutionary solution, the result of joint research and development by the author of the article, who has many inventions in the field of medical devices

with Prof. Dan Adler from the Jet Engine Department at the Faculty of Aeronautics in the Israeli Technion.

And here is the solution:

Revolutionary low cost, instructions free VibraMeshTM Dry Powder Inhaler (VDPI)– having >90% Lung Particles Deposition.

The Solution

CanDapi revolutionary DPI is based on a VibraMeshTM technology activated only when the patient inhales; creating a high-frequency vibration of an internal leaf. The vibrations shake the drug chamber, which is covered by a sieve. The vibrations break powder agglomeration and release particles at a specific size that is streamed to the lungs until all powder is consumed. The device achieved the highest score of lung particle deposition scores vs. competitors during the development of the prototypes (~80% efficiency, Kiel University, Germany)7,8 and 91.8% with cannabinoids dry powder as tested by Copley lung simulator. The patient can breathe through the device with the lowest known airflow resistance without special warnings. The cost of the inhaler without the drug is less than 2€.

Key Message

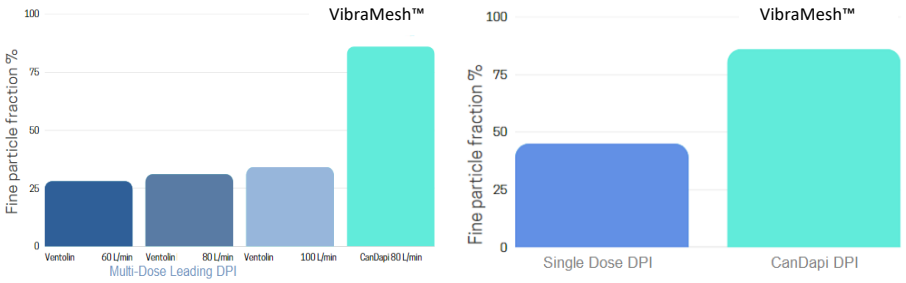
The most important finding of The VibraMeshTM DPI:

- The most important finding of The VibraMeshTM DPI
- >90% efficiency
- Works only during inhaling (breath through DPI).
- Lowest air-flow resistance (0.01 KPa1/2/ l/min)
- Simple and easy-to-use DPI
- Suits everyone – Multi-age and disabled patients
- Customizable
- delivery of soluble cannabinoid powder
- Very low cost
- Very long shelf life

Works only during inhalation and stops vibrations and operation during exhalation.

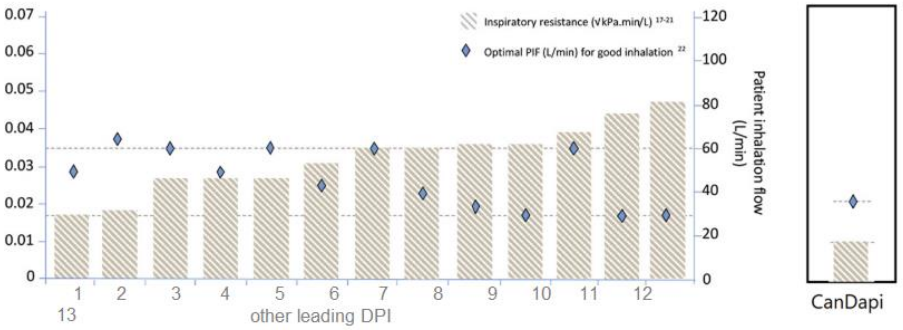
Summary of the scientific technology solution and testing results and achievements

Efficacy Test Results



Comparison of Fine particle others to CanDapi DPI

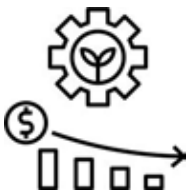
Dose DPI: Air-flow Resistance Test



Analyzing VibraMeshTM air-flow resistance by Copley DFM4 – Flow Meter vs. Others[9]

De-agglomeration

According to "The Investigation of the "New Single-Use Dry Powder Inhaler" by Wagenseil, L., Menge, and Steckel, H. Department of Pharmaceutics and Biopharmaceutics, Christian Albrecht University, Grasweg 9a, 24118 Kiel, Germany, the VibraMeshTM Dry powder inhalers are well-established in the treatment of various lung diseases and are also useful for systemic drug delivery. They can simply be adapted to the requirements of a single use device, which provides several advantages such as application in acute therapy, economic integration into treatment regimen in hospitals and once-only use. Therefore, preferred features of a disposable device are, amongst others, a low resistance, an effective powder de-agglomeration and a constant powder release at clinically relevant air flow-rates. Intuitive and simple use of the device is essential as well. The de-agglomeration efficiency of the device was calculated in percentage based on the obtained primary particle size distribution, which was assumed to be 100% de-agglomerated.

Grandma sifting flour	Clarinet single reed diffuser	Minimum airflow resistance and creating a "jet" air stream based on aeronautical principles	Low-cost materials and manufacturing
			

The scientific principles

Cannabinoids VibraMeshTM Test Results

Note: The cannabinoids formulation is a water-soluble dry powder.

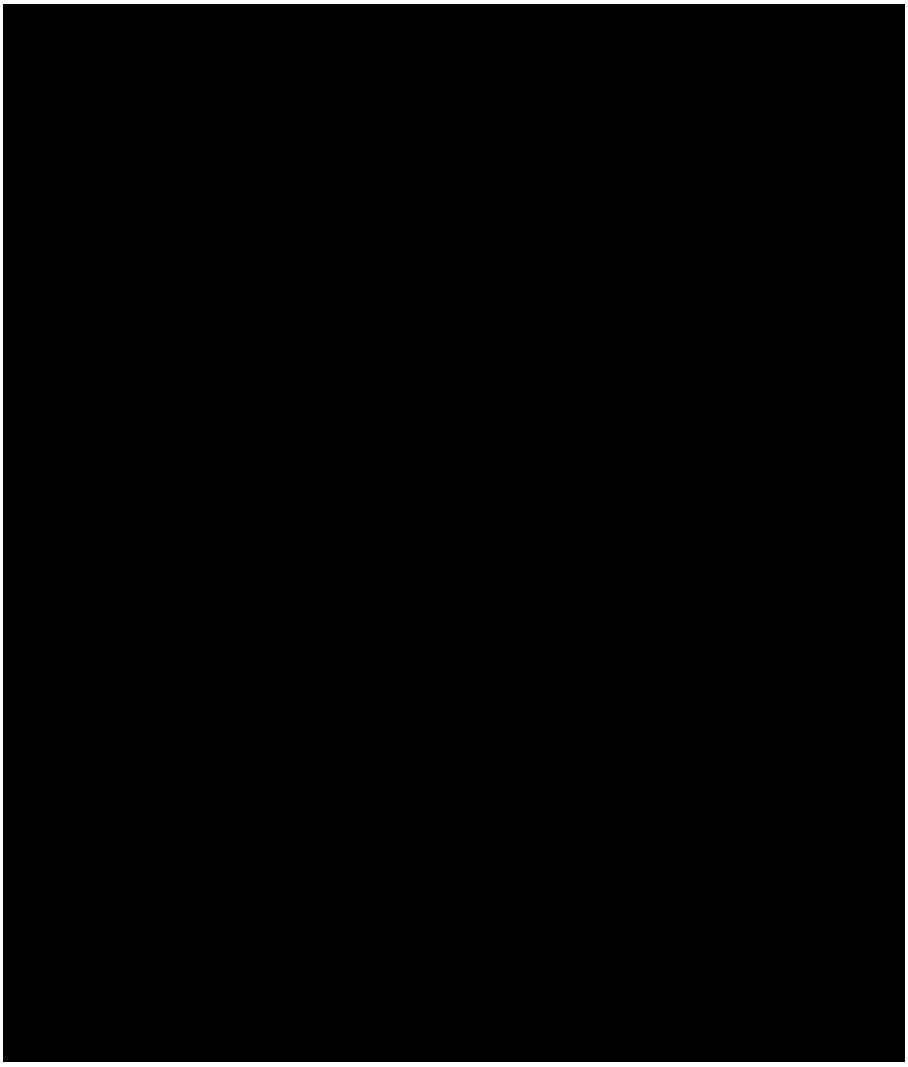
Test Material	Powder type	Amount Loaded (mg)	Total amount released (mg)	Total amount released (%)
THC 1	High THC	5.52	5.07	91.8

- *> 90% of the cannabinoid-lactose formulations material was released from the ESD*
- *No increase in degradation, photodegradation or oxidation products in comparison to control (d8-THC, CBL or CBN).*
- *Cannabinoid profile remain with no change.*
- *Cannabinoids powder DPI test results shows excellent performance*

Conclusion

The patented DPI based on VibraMeshTM, solved four major issues of the existing DPI:

1. Efficiency
2. Solving high airflow resistance issues
3. Solving DPI powder agglomeration issues
4. Simplicity of use for all ages and medical condition
5. Price for the end user, the healthcare provider and a solution for developing countries
6. Replacing harmful cannabis cigarettes and cannabis VAPEs with safer DPI solution



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Amnon Kritzman Kadron

Amnon Kritzman Kadron, Founder and Inventor, Engineer (M.Sc.) From the Technion, Israel. Amnon is a serial entrepreneur and inventor with over 20 patents. CEO and CTO of several medical devices and biotechnology engineering companies based on his inventions. Amnon is currently the CEO and founder of CanDapi in Israel based on his invention of the innovative new Dry Powder Inhaler (DPI).