SPEAKER SPOTLIGHT:

Inhaled Therapy Formulations For Alternative Therapeutic Areas

Due to the prevalence of chronic respiratory diseases, the inhalation industry is striving to develop nasal and pulmonary formulations and devices. Through the optimisation of combination products and advances in emerging therapeutic areas, pharma and academia are driving positive changes in patient adherence and technique. Enjoy our interview with Dr. Pavan Muttil and keep up to date with the latest fast-moving developments in inhaled antibiotics and formulation techniques for inhaled combination therapies.

Pavan Muttil

Associate Professor, Pharmaceutical Sciences, **University of New Mexico**

Dr. Muttil is an Associate Professor with tenure in the Department of Pharmaceutical Sciences at the University of New Mexico (UNM), New Mexico, USA. He has research experience in aerosol formulation and characterization, and pulmonary delivery of drugs and vaccines in preclinical models. For more than 15 years, he has used the spray drying technique to formulate dry powders; these dry powders, containing both drugs and vaccines, have been evaluated by the pulmonary route of administration in various animal models. Towards his research endeavors, Dr. Muttil has received funding from various grant agencies including, Bill and Melinda Gates Foundation Grand Challenges Exploration, National Institute of Health (USA) and the Defense Threat Reduction Agency (DTRA-USA). In addition, he is the chair of the admissions committee for the Pharm. D. Program in the College of Pharmacy at UNM and is passionate about student mentoring at various levels of education. Dr. Muttil received his bachelor's in pharmacy from the Dr. K.N. Modi Institute of Pharmaceutical and Educational Research, master's in pharmacy from the Birla Institute of Technology & Science, Pilani, and PhD in Pharmaceutics from the Central Drug Research Institute, Lucknow, India. He did post-doctoral research in aerosol drug and vaccine delivery at the University of North Carolina, Chapel Hill before joining UNM.

Could you describe the current focus of your work in inhaled particle formulation?

My laboratory has been developing inhaled drug formulations, containing single or multiple drug in combinations, for infectious diseases such as tuberculosis (TB) and non-tuberculous mycobacteria (NTMs). The particles are formulated using the spray drying technique that are engineered to generate appropriate particle size for pulmonary delivery. The goal of such formulation and development is to develop inhaled products that are safe and efficacious when administered into the lung of patients. Therefore, the drug(s) and the excipient(s) used need to by safe when they are combined into an inhaled dry powder formulation. In addition, my laboratory is developing novel vaccines that can be delivered by the pulmonary route. The lungs are not only a good portal of entry for drugs, but also an organ that is capable of generating an immune response that can protect against many infectious diseases.

What are the key benefits of optimising spray drying techniques?

I have been working on inhaled particle formation for more than 15 years using the spray drying technique. In the past, we had utilized the 2-fluid spray drying nozzle for our inhaled formulation and development; it allowed a single solution (or suspension) to be spray-dried along with an inert gas. My laboratory has spray dried a single drug, or up to four drugs, in one formulation. Although a 2-fluid nozzle allows us to incorporate multiple drug combinations in a single formulation, it has its limitations. Multiple drugs, sometimes may not be compatible when mixed together prior to spray drying. In such a scenario, using a 3-fluid nozzle could potentially overcome drug-in-compatibility concerns; it allows two incompatible drugs to be formulated into a single inhaled formulation. Further, we are currently studying the role of a 3-fluid nozzle in encapsulating a drug within a particle that is appropriate for inhalation. Therefore, using a 3-fluid nozzle allows us to be more innovative with regards to the agents that can be incorporated in our inhaled formulation. Such novelty can be applied to not only antibiotics but also vaccines and biologics.

What have been the biggest challenges that you have faced when developing an inhaled antibiotic?

There are always challenges that need to be overcome during the formulation and development of inhaled antibiotics for infectious diseases. As mentioned above, incompatibility between single (or multiple) drugs along with the excipients used is the foremost challenge. Once formulated, my laboratory also evaluates the stability of the formulation during storage. This is important, since these inhaled antibiotics may be required to be used in low and middle income countries that lack a continuous cold-chain facility for storing and transporting these medicines. In the past, we have successfully overcome some of these hurdles to develop inhaled antibiotics. The next step, and one of the most challenging, is to show the safety and efficacy of inhaled formulation in animal models (preclinical testing). This has been challenging for most researchers working in this field; inhaled animal testing is not as simple as evaluating an oral or injectable formulation. Researchers working in the inhaled formulation field sometimes are not aware of the complexity, and the significant differences between animals and humans when evaluating inhaled drug delivery. Earlier this year, we had published an article that describes the challenges and limitations of using animal models for testing and developing inhaled antibiotics (*Price, D. N., N. Kunda and P. Muttil (2019). "Challenges associated with the pulmonary delivery of therapeutic dry powders for preclinical testing." KONA Powder and Particle Journal*). Proper animal testing is critical, since our ultimate goal is to use animal models to predict the safety and efficacy of inhaled products in humans.

What are some priorities for your work on developing inhaled therapies over the next year?

As mentioned in response to the first question, my laboratory is actively developing inhaled therapies (antibiotic, vaccines and immunotherapies) for various diseases including tuberculosis, NTMs, and lung cancer. As the medical community is understanding the role of inhaled therapies for various diseases, funding agencies around the world are putting their bet in new formulations that can be administered directly into the lung. In 2012, I was awarded a Bill and Melinda Gates Foundation grant to develop an inhaled vaccine for TB. We were able to successfully develop a spray dried TB vaccine; not only will an inhaled vaccine be 'needle-free', since needles and syringes will not be required to administer such a vaccine on a large scale, these vaccines also maintained its potency for long periods without refrigeration. This becomes critical during a mass immunization setting especially in countries that cannot afford the expensive cold-chain. In the last few years, beyond developing novel inhaled antibiotics, my laboratory is also developing inhaled vaccines, inhaled host-directed therapies (HDT), and immunotherapies for many diseases.

How do you see the inhalation field developing in the future?

I see a lot of promise for researchers working in the inhalation drug development field. Although, inhaled therapy has been successful for more than half a century for diseases such as asthma and chronic obstructive pulmonary disease, we are developing novel inhaled formulations for other diseases especially in the infectious diseases realm as we understand more about such diseases. I am therefore excited to explore some of these opportunities, along with many other researchers who are taking the inhalation field to the next level.