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Summary

Pulmonary drug delivery is an attractive way of introducing medication for lung diseases like asthma and COPD and lactose is a widely used carrier particle for pulmonary drug delivery. Physico-chemical properties of carrier particles are thought to play a crucial role in determining the performance of carrier-based dry powder inhalation. Addition of fines (small particles of lactose) has been reported to result in an improved fine particle dose or fine particle fraction of the active drug. However, the mechanism by which the fine particles alter the performance of the formulation has remained elusive. The effects of addition of fines on the surface energy, and more importantly the surface energy distribution, of lactose crystals, as measured by inverse gas chromatography (IGC) is presented here. A new methodology based on finite concentration measurements is reported for surface energy heterogeneity determination. This study reveals that the addition of fines resulted in lactose particles with higher surface energy, contrary to popular hypothesis of passivation of high energy sites by fine excipient particles. The blends were, however, relatively more homogeneous. Such detailed surface energy distribution information may enable the understanding of mechanism behind improved pulmonary drug delivery and lead to optimisation of formulation.

52. DRUG DELIVERY SYSTEMS AND CONSUMER PERCEPTIONS: AN INDIAN VIEWPOINT

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Summary

There is a virtual explosion of inhalational devices in India over the last decade. Different companies trying to create space for their products claim different advantages and plus points over their competitors. How does the patient perceive this profusion of devices? Does this depend on symptom relief and efficacy, improved quality of life or cost advantage or severity of disease? A six-point questionnaire was devised and tested in about 200 patients who were already using these devices for last 3 months and the perception variables were sought to be defined objectively. The questionnaires were peer reviewed by 3 pulmonologists, administered by a clinical assistant having a certain rapport with patients and having enough orientation towards the various Inhalational devices in the Indian market. Multiple patients related variables were sought to be addressed including possible apathy to a gadget amongst a population with high illiteracy prevalence. Patient perception and hierarchy of needs, however is far more complex than can be elucidated in an interview with questionnaire survey. It is multi factorial no doubt but does not only depend on cost benefit analysis but also on individual variables and disease variables. There are obvious imitations to this approach and much will depend on individual markets their complexities including cultural and social variables. This study tries to measure some of these variables at a time when the Indian inhaler market is virtually exploding for various reasons beyond control of either the prescribing doctors or the consumer patients.

53. GREAT EXPECTATIONS — THE STORY OF AN ORPHAN'S PROGRESS

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Summary

Delivering certain drugs via oral inhalation may allow for greater efficacy and safety in the treatment of a number of medical conditions. Over the last 50 years a wide variety of systemic and lung diseases have seen the application of inhaled therapies for conditions as diverse as Asthma, Diabetes Mellitus and immunisation against Measles. Fuelling this trend has been a greater understanding of lung pathology, physiology, delivery technologies and the discovery of some novel therapeutic options requiring "topical" application such as gene therapy and interference RNA. This presentation will review the use of oral inhalation technology in one commonly encountered situation, namely immunisation. In particular the use of a mucosal vaccine for Measles where in one study conducted in over 3 million children in Mexico attack rates were reduced from 14% in the group receiving vaccination via the injection route to 0.8% in those receiving a wet nebulised live attenuated preparation. It will then explore the role for orally inhaled medicines in two orphan indications; immunosuppression in lung transplantation where an inhaled version of ciclosporin has already been the subject of clinical investigations and finally, the prevention and treatment of fungal lung infection where work is at an earlier stage.

54. EFFERVESCENT INHALABLE NANOPARTICLES FOR TREATING LUNG CANCER

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Summary

The use of effervescent aerosol carrier particles to deliver and then actively release doxorubicin nanoparticles in the lungs is examined as a treatment for lung cancer *in vivo* in Balb/c mice. Comparison against control groups with noneffervescent carrier particles, as well as nonaerosol delivery by iv injection of either doxorubicin nanoparticles or solution, as well as no treatment, is made. The aerosolized formulations were prepared using spray freeze-drying to produce respirable aerosols. Survival curves were determined for each treatment group. Treatment with effervescent doxorubicin nanoparticle powders resulted in improved survival when compared with the other control groups. In particular, survival of >80% at 90 days, and >70% at 140 days (the end point of the study) was found. In contrast, all mice died in less than 50 days when treated with iv injection of either doxorubicin solution or doxorubicin nanoparticles. In addition, compared to the effervescent nanoparticle powder inhalation group, the lungs of animals in the control groups showed larger and more numerous tumors in pathological samples. Magnetic resonance imaging corroborated the pathology results. Our findings show that effervescent doxo-

rubicin nanoparticle powder appears highly promising as a non-invasive means of treating lung cancer.

55. OVERCOMING THE CHALLENGES OF INHALER USE IN CHILDREN

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Summary

Asthma is the most common chronic disease of childhood and 80% of pediatric asthma cases are diagnosed before the age of six. Despite advances in care and effective therapies like inhaled corticosteroids, poor asthma control is still common. One of the primary factors contributing to this is the poor efficiency of inhaled drug delivery resulting from the inability of young children to correctly use inhalers. Young children, especially those below the age of six have the following limitations that create obstacles to effective inhaler use: anatomical and physiological, cognitive, verbal, coordinative and emotional. An 'active' dry powder inhaler is discussed designed with features to overcome many of these limitations, and in particular the inability of young children to understand and to coordinate a proper breathing maneuver. To address this particular limitation, an inhaler prototype was designed that incorporates a visual feedback system linked to a directional flow sensor and based on 'cause and effect' principles to help guide children through a proper inhalation maneuver. Additionally, the inhaler incorporates specific flow resistance designed to aid in slowing down, or prolonging the child's inhalation. An informal user study was performed with 8 children ranging in age from 3 to 6 years with this prototype system and further incorporating spirometry to measure and capture each child's inhalation profile. The study demonstrated that with visual feedbacks tied to their inhalation maneuver, and with minimal training, children as young as 3 years were able to consistently generate sufficient inhalation flow rates (>15 L/min) of sufficient duration (>1 second) to deliver a simulated pediatric dose.

56. DRIVING COST EFFECTIVENESS THROUGH PATIENT CENTRIC DPI DESIGN

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Summary

In recent years increasing focus has been directed at the cost of treatment due to the pressures placed on health care systems combined with the growing prevalence of asthma and chronic obstructive pulmonary disease (COPD). Patient compliance is a major contributor to poor disease control and can be linked to both willingness to follow the treatment regimen and ability to use the prescribed inhaler. Thus inhaler design can have a significant impact on a patient's ability to be compliant.

An example of patient centric design is illustrated using research conducted during the development of the 3M™ Taper Dry Powder Inhaler (DPI). A four stage research project was conducted with asthma/COPD patients (children, adults and the elderly), specialist respiratory nurses and pharmaceutical developers. This provided a detailed understanding of the main drivers and expectations for each group and enabled testing of different forms, features and concepts. The results of the research were fed directly into the Taper development programme enabling device design to meet both the user needs and the technical requirements of a high performing DPI.

57. TREATMENT OF PATIENTS WITH SEVERE PULMONARY ALVEOLAR PROTEINOSIS USING INHALED GM-CSF DELIVERED VIA THE I-NEB AAD SYSTEM

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Summary

Pulmonary Alveolar Proteinosis (PAP) is an extremely rare disease which is characterized by the accumulation of lipoproteinaceous surfactant component material in the alveolar spaces. In most cases this results from an antibody mediated non-expression of granulocyte monocyte colony stimulating factor (GM-CSF). The current mainstay of treatment is massive whole lung lavage (WLL). Better understanding of the patho-physiology of PAP has led to new treatments, including exogenous GM-CSF either by injection (systemic), or the inhalation of aerosol (iGM-CSF). From November 2006 all patients at the Royal Brompton Hospital with proven PAP that was not in lasting remission after a cycle of 6 WLL treatments were considered for a trial of iGM-CSF. All cases were discussed by a multi-disciplinary team. Each patient was trained in the correct use of the I-neb AAD (Adaptive Aerosol Delivery) System, which was selected due to its efficient drug delivery. Each patient then had four treatment days with 250μg iGM-CSF per day, followed by four rest days. This cycle was repeated ad infinitum. An assessment was conducted at 3 month intervals to check for clinical response/improvement or the need for further WLL. The dose of iGM-CSF was gradually reduced. All five patients showed significant improvement in objective and subjective measures (dyspnea, exercise tolerance, PFTs, oxygen requirements, a dramatic reduction in the need for WLL and no further requirement for supplemental oxygen. Four patients did not require WLL during the course of the study. The remaining patient had a diminishing need for WLL over 6 months, then no further WLL for the remainder of the study. No side effects or adverse events were observed. Treatment with iGM-CSF resulted in a long-lasting improvement in clinical measures and the elimination of need for further WLL in a group of patients with severe PAP, whom had previously required multiple WLL treatments. This reduction in WLL resulted in increased convenience for the patient.

58. RAPID CHARACTERISATION OF OINDPS USING AUTOMATED IMAGE ANALYSIS AND MORPHOLOGICALLY-DIRECTED RAMAN SPECTROSCOPY

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