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| **Effect of nebulised BromAc®, a potent mucolytic, in a mechanically ventilated ex-vivo muco-obstructive ovine lung model.** |
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| **Introduction**- Mucus plugging of the respiratory tract occurs in airway diseases, including asthma, chronic obstructive pulmonary disease and cystic fibrosis. It can cause partial or complete blockage of airways, leading to breathlessness and respiratory failure. Here, we demonstrate the mucolytic effect of BromAc® in dissolving mucus simulant in an ex-vivo ovine muco-obstructive lung model.  **Method-** A mucus simulant was prepared from soft mucin extracted from Pseudomyxoma peritonei (PMP) during surgical tumor resection was mixed with phosphate-buffered saline (PBS) to obtain a viscous consistency seen in cystic fibrosis (Viscosity~20,000 mpa.s). The mucus simulant was filled into the trachea of freshly slaughtered ovine lungs and ventilated via endotracheal tube (ETT) using Continuous Mandatory Ventilation (CMV). Predetermined single or repeated doses of Bromelain, Acetylcysteine (Ac), BromAc® (Bromelain and Ac formulation) and saline (control) were administered via an Aerogen® vibrating nebuliser and ventilated with a humidified circuit for 30 or 60-minute time point. Real-time ventilatory recording, including airway resistance, compliance, tidal volume, and rheology measurements, was carried out.  **Result-** A significant decline in airway resistance (p<0.0001) compared to saline control was observed over time when treated with Bromelain, Ac and BromAc®, with the latter showing a stronger mucolytic potency than single agents. The decline in airway resistance was also effective in a shorter time-point and at lower doses of the agents than saline control(p<0.01). Similar effects of BromAc® in maintaining tidal volume were recorded in a sixty-minute time point study. Rheology measurements revealed that BromAc®™ significantly reduced the viscosity of the mucin at both 30-minute and 60-minute time points (p<0.0001) compared to saline control. When single agents and lower concentrations were trialled, the effect on resistance and viscosity was less than the combination.  **Conclusion-** BromAc® showed complete dissolution of the respiratory mucus simulant and improved ventilatory airflow parameters in the ex-vivo ovine model.  **Grant Support:** The study is financially supported by Mucpharm Pty Ltd, Kogarah, NSW, Australia |