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PED4 inhibitor-loaded phosphatiosomes for attenuating neutrophilic inflammation in acute lung injury

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Cilomilast is a Phosphodiesterase 4 (PDE4) inhibitor for treating inflammatory lung diseases. This agent has a narrow therapeutic index with significant adverse effects on the nervous system. This study was conducted to entrap cilomilast into PEGylated Phosphatidylcholine (PC)-rich niosomes (phosphatiosomes) to improve pulmonary delivery via the strong affinity to pulmonary surfactant film. Neutrophils were used as a cell model to test the anti-inflammatory activity of phosphatiosomes. In an *in vivo* approach, mice were given Lipopolysaccharide (LPS) to produce Acute Lung Injury (ALI). The surface charge in phosphatiosomes that influenced the anti-inflammatory potency is discussed in this study. The average diameter of the phosphatiosomes was about 100 nm. The zeta potential of anionic and cationic nanovesicles was -35 and 32 mV, respectively. Cilomilast in both its free and nanocapsulated forms inhibited superoxide anion production but not elastase release in activated neutrophils. Cationic phosphatiosomes mitigated calcium mobilization far more effectively than the free drug. *in vivo* biodistribution evaluated by organ imaging demonstrated a two-fold ameliorated lung uptake after dye encapsulation into the phosphatiosomes. The lung/brain distribution ratio increased from 3 to 11 after nanocarrier loading. The intravenous nanocarriers deactivated the neutrophils in ALI, resulting in the elimination of hemorrhage and alveolar wall damage. Only cationic phosphatiosomes could significantly suppress IL-1 β and TNF- α in the inflamed lung tissue. These results suggest that phosphatiosomes should further be investigated as a potential nanocarrier for the treatment of pulmonary inflammation.

Biography

Jia-You Fang is currently a Professor in the Graduate Institute of Natural Products at Chang Gung University in Taiwan. In addition, he is an Adjunct Professor in the Graduate Institute of Health Industrial Technology, Chang Gung University of Science and Technology and Department of Anesthesiology, Chang Gung Memorial Hospital. Over the past 25 years, he and his team have made contributions to the understanding of drug delivery, pharmaceuticals, pharmacokinetics, nanomedicine and cosmetology. His contributions add up to 249 peer-review articles, more than 6000 citations and H index of 44.

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