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Disposition of Alpha-1-Antitrypsin in the Isolate Perfused Rabbit Lung

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Abstract:

The potential for delivering large molecular weight proteins into the lungs to reach local or systemic sites of action was investigated by examining the disposition of alpha-1-antitrypsin in the isolated rabbit lung. Alpha-1-antitrypsin, a model protein, was measured in the perusion medium following intravascular administration and was found to remain constant, indicating limited uptake or metabolism by lung tissue. Intrabronchial instillation of 10 mg of alpha-1-antitrypsin in water resulted in no measurable concentration in the recirculating perfusate during the two hours experiment. These data suggest that transport of large proteins may be limited across lung-blood membrane barriers in either direction. Though this would limit the ability of inhaled drugs with large molecular weights to reach the general circulation, proteins which are used to treat respiratory diseases, such as alpha-1-antitrypsin, might be delivered locally by inhalation with only negligible systemic exposure.

Keywords:

[Alpha-1-Proteinase Inhibitor](#) . [Pulmonary absorption](#) . [Isolated perfused rabbit lung](#)

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