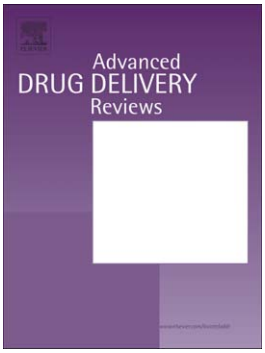

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Targeted Pulmonary Delivery of Inducers of Host Macrophage Autophagy as a Potential Host-Directed Chemotherapy of Tuberculosis

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Abstract

One of the promising host-directed chemotherapeutic interventions in tuberculosis (TB) is based on inducing autophagy as an immune effector. Here we consider the strengths and weaknesses of potential autophagy-based pharmacological intervention. Using the existing drugs that induce autophagy is an option, but it has limitations given the broad role of autophagy in most cells, tissues, and organs. Thus, it may be desirable that the agent being used to modulate autophagy is applied in a targeted manner, e.g. delivered to affected tissues, with infected macrophages being an obvious choice. This review addresses the advantages and disadvantages of delivering drugs to induce autophagy in *M. tuberculosis*-infected macrophages. One option, already being tested in models, is to design particles for inhalation delivery to lung macrophages. The choice of drugs, drug release kinetics and intracellular residence times, non-target cell exposure and feasibility of use by patients is discussed. We term here this (still experimental) approach, of compartment-targeting, autophagy-based, host-directed therapy as "Track-II antituberculosis chemotherapy."

Keywords

Inhalations, aerosols, host-pathogen interaction, phagocytosis, apoptosis, microautophagy