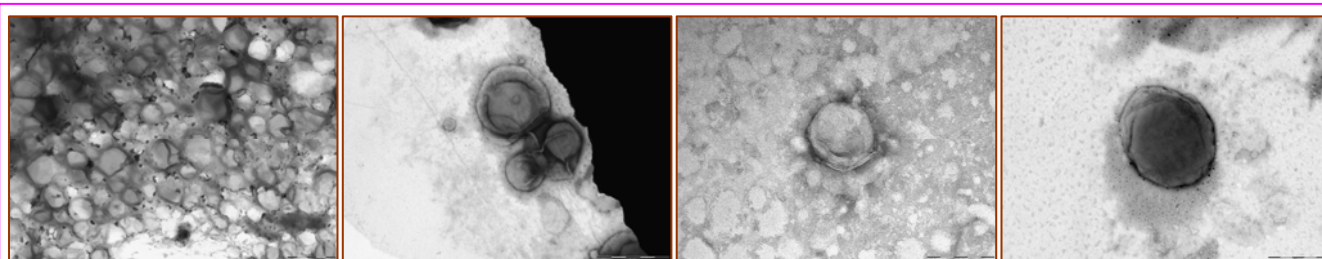


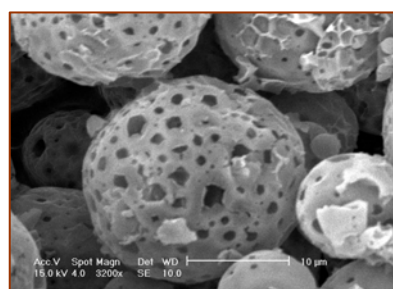
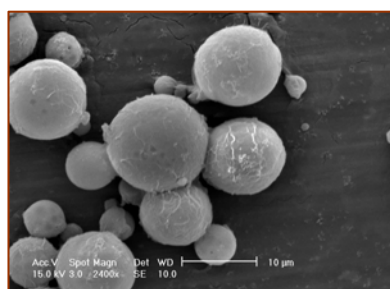
Pulmonary delivery of antitubercular drugs

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Capreomycin is a potent antitubercular drug whose therapeutic utilization is limited by its high toxicity. The development of new formulations by employing specific carriers may reappraise its use by preserving its activity and reducing its side effects. This approach can be useful for improving the existing therapies which are difficult and sometimes ineffective. The present project is aimed at the development of new microparticle and liposome based capreomycin sulphate formulations, by assessing new strategies to obtain safe and effective products for inhalation.



Capreomycin loaded Liposomes



Capreomycin loaded PLGA microparticles

1. Description of the product

Capreomycin sulphate (CS) is a highly toxic second line antitubercular drug, active against multi-resistance strains. CS encapsulation into new drug delivery systems such as microparticles and liposomes may allow reappraisal of its therapeutic usefulness by reducing its side effects and keeping up its biological activity. Pulmonary delivery is potentially the most suitable route as it implies CS high local concentrations and make possible its intracellular targeting. In this way the uncontrolled distribution of the drug into the organism can be limited. CS high hydrophilicity makes necessary a deep study to find the optimal preparation conditions in order to develop inhalable formulations and to maximize drug content into the final products.

2. Innovative aspect of the product

CS modified release formulations such as microparticles and liposomes indeed represent a new approach in delivering such peptide. In fact, to date, only parenteral solution for injection (Capastat® sulfate) is available on the market. CS formulation as microparticulate system potentially inhalable may allow drug pulmonary administration, which so far has not been employed in antitubercular therapy.

3. Main advantages of the offer

CS is administered in high doses, by i.v. injection, over 60 minutes, or deep i.m. injection into a large muscle mass. Current treatments require administrations over an extended period of time. This results in serious

adverse effects such as ototoxicity, nephrotoxicity and dose related eosinophilia and leads to clinical failure. Therefore, developing a new inhalable formulation may represent an important step forward in the CS antitubercular therapy. In fact, the inhalation of CS delivery systems can offer several advantages: i) increased local lung drug concentration for given dose, ii) drastic reduction of dose and systemic exposure with a consequent more efficacious and tolerable therapy, iii) facilitated intracellular delivery, particularly to alveolar macrophages and lymphocytes, iv) ease of delivery.

In addition such formulation may be more prone to macrophage uptake if compared to CS inhalable powder. Furthermore, the aerosol formulation does not require extensive training of health-care workers to follow the therapy, minimizing the need for added personnel. All these features along with the increased product safety will enhance patient's compliance and adherence to therapy and potentially reduce the disease burden to both patients and population.

This strategy, therefore, could support reappraisal of an efficacious drug otherwise limited to a second-third line role, thus increasing the chance for a successful therapy in MDR cases.

4. Technology key words

Capreomycin, Liposomes; Microspheres, Inhalation; Tuberculosis; Pulmonary delivery

5. Current Stage of Development

Development phase – laboratory tested

6. Intellectual Property Rights

Copyright protected

Technical and scientific publications

S. Giovagnoli, D. Songara, P. Blasi, M. Ricci, L. Perioli, C. Rossi, Preparation and characterization of respirable biodegradable microspheres for capreomycin pulmonary delivery 12th International Pharmaceutical Technology Symposium September 12-15, 2004 Istanbul/ Turkey p. 73.

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