Formulasi, Karakterisasi dan Uji Sitotoksisitas Serbuk Kering Inhalasi Rifampisin dengan Pembawa Kitosan-Alginat = Formulation, Characterization and Cytotoxicity Test of Rifampicin Dry Powder Inhalation with Chitosan-Alginate as Carrier

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Abstrak

Tuberkulosis (TB) merupakan penyakit infeksi yang disebabkan oleh Mycobacterium tuberculosis, salah satunya menginfeksi saluran pernafasan. Penghantaran obat rifampisin sebagai salah satu antibiotik pengobatan TB melalui rute pulmonar yang menargetkan langsung paru-paru dan alveolus diharapkan dapat memberikan hasil yang lebih efektif dan efisien, sehingga dibutuhkan rifampisin dalam bentuk inhalasi. Penelitian ini bertujuan untuk memformulasi serbuk inhalasi rifampisin dengan variasi komposisi pembawa kitosan-alginat, mengevaluasi karakteristik, profil pelepasan obat dan sitotoksisitas Serbuk kering inhalasi dibuat dengan menggunakan metode semprot kering. Serbuk yang dihasilkankemudian dianalisis ukuran partikel, bentuk, kandungan lembab, kadar obat, dan rendemennya. Laju pelepasan rifampisin dalam medium dapar fosfat pH 7,4 dan SLS 0,05%, dan dalam medium dapar KHP pH 4,5 serta sitotoksisitasnya terhadap cell line A549 juga dievaluasi. Hasil penelitian menunjukkan bahwa formula F3 (dengan kitosan-alginat 1:1) dinilai sebagai formula dengan profil disolusi terbaik, yaitu pada 120 menit dalam dapar fosfat pH 7,4 dan 0,05% SLS sebesar 78,301±1,332 % dan dalam dapar KHP 4.5 sebesar 41.355±1,259 %. Formula F3 tersebut memiliki rentang ukuran partikel geometris 342-955,4 nm (IPD 0,104) dan ukuran partikel aerodinamis 11,4288±1,259 µm. Hasil disolusi membuktikan kitosan-alginat dapat meningkatkan laju pelepasan rifampisin sehingga memiliki sitotoksisitas yang lebih rendah terhadap sel epitel paru. Formula F3 terbukti masih aman terhadap sel epitel paru (viabilitas 89,73%) pada konsentrasi hingga 0,1 mg/mL.
.....Tuberculosis is an infectious disease caused by Mycobacterium tuberculosis that could infect respiratory tract. Pulmonary drug delivery system of rifampicin, as one of the antibiotics used to treat TB, is expected to provide more effective and efficient results as it is directly targeted into the lungs and alveoli. This study aimed to formulate rifampicin inhalation powder with various ratio of chitosan-alginate as carrier, as well as evaluate its characteristics, drug release profile and its cytotoxicity. Dry powder inhalation was prepared using spray dry method. The obtained powder was then analyzed for its particle size, morphology, moisture content, drug content, and yield. Drug release profile in phosphate buffer medium pH 7.4 and SLS 0.05%, and in buffer medium KHP pH 4.5, as well as its cytotoxicity towards cell line A549 were also evaluated. The results showed that F3 (with chitosan-alginate 1:1) was considered as formula with the best dissolution profile in medium pH 7.4 and pH 4.5. It showed the drug release in medium pH 7.4 and pH 4.5 were 78.301±1.332 % and 41.355±1.259 %, respectively. Powder F3 also possessed range of geometrical particle size of 342-955.4 nm (PDI 0.104) and aerodynamical particle size of 11.4288 ± 1.259 µm. Drug release testing showed that combination of chitosan-alginate as carrier improve rifampicin drug release in both medium, thus showed lower cytotoxicity toward pulmonary epithelial cells. Powder F3 was considered as safe toward pulmonary epithelial cells (viability 89.73%) in concentration up to 0.1 mg/mL.