Optimasi Formula dan Proses Produksi Serbuk Inhalasi Rifampisin-Manitol = Formula and Production Process Optimization of Rifampicin-Mannitol Dry Powder Inhalation

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Abstrak

Serbuk inhalasi rifampisin-manitol (1:1) diketahui mampu meningkatkan kelarutan rifampisin dalam medium cairan paru dan penambahan L-leusin 30% b/b mampu memperbaiki sifat aerodinamis serbuk inhalasi rifampisin. L-leusin bersifat hidrofobik sehingga perlu diketahui konsentrasi optimalnya yang dapat menghasilkan serbuk dengan sifat aerodinamis terbaik tanpa menurunkan kelarutan rifampisin. Parameter produksi, seperti kecepatan penyemprotan dan tekanan gas atomisasi dapat mempengaruhi hasil dan karakter serbuk inhalasi yang dihasilkan. Penelitian ini bertujuan untuk memperoleh formula optimum serbuk inhalasi rifampisin dengan pembawa manitol (1:1) dan penambahan L-leusin menggunakan Response Surface Methodology (RSM). Formula optimum diharapkan dapat menghasilkan serbuk inhalasi dengan rendemen di atas 70%, Fine Particle Fraction (FPF) di atas 50%, persentase serbuk teranalisis (Emitted Fraction/EF) di atas 50%, dan persentase rifampisin terdisolusi di atas 50%. Lima belas formula percobaan dirancang secara statistik menggunakan desain Box Behnken dengan memvariasikan tiga parameter, yaitu konsentrasi L-leusin, kecepatan penyemprotan, dan tekanan gas atomisasi. Serbuk diformulasikan menggunakan metode semprot kering lalu dikarakterisasi fisik dan kimianya. Serbuk inhalasi yang diperoleh dari 15 formula tersebut menghasilkan rendemen 49–73%, diameter aerodinamis pada rentang 0,07 ± 1,38 µm hingga 15,45 ± 1,37 µm, EF sebesar 38,95-50,8%, FPF sebesar 16,44-33,03%, dan persentase rifampisin terdisolusi sebesar 28,51-65,14%. Hasil optimasi menunjukkan bahwa konsentrasi L-leusin optimum adalah 30% b/b, kecepatan penyemprotan optimum sebesar 22,99% atau 6,14 mL/menit, dan tekanan gas atomisasi sebesar 35,36 mm.

.....Rifampicin-mannitol inhalation powder (1:1) is known to increase the solubility of rifampicin in the lung fluid medium and the addition of 30% w/w L-leucine can improve the aerodynamic properties of rifampicin inhalation powder. L-leucine is hydrophobic, so it is necessary to know the optimal concentration that can produce powder with the best aerodynamic properties without reducing the solubility of rifampicin. Pump rate and atomizing gas pressure can affect the yield and character of the inhalation powder produced. This study aims to obtain the optimum rifampicin inhalation powder formula with mannitol carrier (1:1) and the addition of L-leucine using Response Surface Methodology. The optimum formula is expected to produce inhalation powders with yields above 70%, Fine Particle Fraction (FPF) above 50%, Emitted Fraction (EF) above 50%, and the percentage of dissolved rifampicin above 50%. Fifteen experimental formulas were statistically designed using the Behnken Box design by varying three parameters, such as L-leucine concentration, pump rate, and atomizing gas pressure. Powders were formulated using the spray dry method and then characterized physically and chemically. The inhalation powder obtained from these 15 formulas produced a yield of 49–73%, aerodynamic diameter in the range of 0,07 ± 1,38 µm to 15,45 ± 1,37 µm, EF is 38,95-50,8%, FPF is 16,44-33,03%, and the percentage of dissolved rifampicin is 28,51-65,14%. The optimization results showed the optimum L-leucine concentration is 30% w/w, pump rate is 22,99% or 6,14 mL/minute, and atomizing gas pressure is 35,36 mm.