INTISARI

PUTRI, A.,N., 2015, FORMULASI DAN OPTIMASI SEDIAAN TABLET BUKAL *BILAYER* SIMVASTATIN DENGAN POLIMER *CARBOPOL* 934P, HPMC DAN *ENHANCER* POLIETILEN GLIKOL (PEG 6000), TESIS, FAKULTAS FARMASI, UNIVERSITAS SETIA BUDI, SURAKARTA.

Simvastatin dapat menurunkan *Low-Density Lipoprotein Cholesterol* dan meningkatkan *High Density Lipoprotein Cholestrol*. Simvastatin memiliki bioavailabilitas rendah (5%) karena mengalami metabolisme di hati dan waktu paruh 3 jam. Penelitian ini bertujuan membuat sediaan tablet bukal *bilayer* mukoadhesif simvastatin dengan campuran *Carbopol 934P*, HPMC, PEG 6000; mengetahui pengaruh variasi jumlah polimer terhadap sifat fisik dan pelepasan obat, serta mengkaji kemampuan permeasi simvastatin dari formula optimum.

Penentuan formula dengan *factorial design* 2^3 menggunakan *software* Design Expert® sebanyak 8 formula. Pembuatan formula tablet bukal *bilayer* dibuat menggunakan metode *direct compress* terdiri atas *layer* yang mengandung polimer dan obat. *Layer* 2 sebagai *backing membrane* dan mengandung bahan tidak larut air.. Evaluasi uji meliputi, bobot, keseragaman bobot, diameter, ketebalan, kekerasan, *swelling*, lama dan kekuatan perlekatan, keseragaman kandungan, stabilitas fisik dalam simulasi saliva, pH permukaan, kandungan, pelepasan obat secara *in vitro*. Formula optimum di uji karakteristik fisik dan permeasi *ex vivo* melewati bukal kambing selama 8 jam.

Hasil uji menunjukkan bahwa *Carbopol* dan PEG 6000 signifikan meningkatkan *swelling index* dan kekuatan perlekatan, sedangkan HPMC signifikan menurunkan *swelling index* dan kekuatan perlekatan. PEG 6000 signifikan meningkatkan pelepasan obat, sedangkan *Carbopol* dan HPMC signifikan menurunkan pelepasan obat. Jumlah simvastatin yang tertranspor sebesar 22,02±0,14% selama 8 jam, *lag time* 0,05 jam, *fluks* 0,764 $\mu g.cm^{-2}.jam^{-1}$, dan koefisien difusi 0,133 $cm^2.jam^{-1}$. Variasi jumlah polimer *Carbopol 934P*, HPMC, dan PEG 6000 sebesar 9,75%, 20,35%, dan 20,35% dapat digunakan untuk membuat tablet bukal *bilayer* mukoadhesif simvastatin dengan sistem pelepasan diperlama selama 8 jam untuk menghindari *first pass metabolism*.

Kata kunci: simvastatin, *buccal bilayer*, *Carbopol*, HPMC, permeasi

ABSTRACT

PUTRI, A.,N., 2015, FORMULATION AND OPTIMATION BUCCAL MUCOADHESIVE BILAYERED TABLET FORMULATION USING POLYMER MUCOADHESION CARBOPOL 934P, HPMC AND POLYETHYLEN GLICOL (PEG 6000) AS ENHANCER, TESIS, FAKULTAS FARMASI, UNIVERSITAS SETIA BUDI, SURAKARTA.

Simvastatin have the ability to reduce Low-Density Lipoprotein Cholesterol and increase High Density Lipoprotein Cholestrol. Simvastatin has low bioavailability caused by high first-pass metabolism effect, and short biological half-life (3 jam) The purpose of this research was to prepare the mucoadhesive bilayered tablet of simvastatin by using mucoadhesive polymers such as Carbopol, Hydroxy propyl methyl cellulose (HPMC) in different concentration and to determine the influence of count variation of polymer on the physical properties and drug release, as well as assess the ability of simvastatin permeation on the optimized formulation.

The determination of formulas with 2^3 design factorial using Design Expert Software® as 8 formulas. Tablets were prepared by direct compression method. The first layer which adheres to mucosa and containing of mucoadhesive polymers and drug. The second layer as backing membran and contain water impermeable agent. Tablets were subjected for physicochemical characterization test such as weight, weight variation, dimensions, thickness, hardness, swelling index, time and mucoadhesive strength, drug content, in vitro drug release study, surface pH, and stability in saliva simulation. Optimized buccal mucoadhesive bilayered tablet formulation were subjected for in vitro drug permeation through sheep buccal mucosa on 8 hour.

The test results showed that Carbopol and PEG 6000 significantly increase the swelling index and strength adhesions, while the HPMC significantly lower the swelling index and strength adhesion. PEG 6000 significantly increases drug release, while Carbopol and HPMC significantly lowering of drug release. In vitro drug permeation was found 22,02±0,14% in 8h, lag time 0,05h, fluks 0,068 µg.cm^{-2}.hour^{-1}, and diffusion coefficient 7,5 cm^2.jam^{-1}. Mucoadhesive polymers Carbopol, HPMC, and PEG 6000 in various proportions can be used to prepare buccal mucoadhesive bilayered tablet of simvastatin.

*Key: simvastatin, buccal bilayer**,** Carbopol, HPMC, permeation*