INTISARI

Setiap tindakan implantasi yang menimbulkan luka terbuka selalu direspon oleh tubuh dengan proses penyembuhan luka termasuk reaksi inflamasi yang menimbulkan rasa sakit pasca operasi. Pada umumnya dokter akan memberi resep obat *non steroid anti-inflammatory drug* (NSAID), salah satunya adalah aspirin. Efek samping penggunaan obat NSAID peroral adalah terjadinya ulkus peptikum. Tujuan penelitian ini adalah mengubah rute pemberian aspirin secara peroral menjadi rute lokal dengan cara pemuatan aspirin ke dalam perancah hidrogel gelatin $CaCO_3$ sesuai dengan prinsip *Drug Delivery System* (DDS) sebagai solusi agar aspirin berefek lebih kuat dan lebih cepat di daerah target, memiliki kemampuan *prolonged release* sehingga mengurangi efek samping sistemik dan menurunkan toksisitas lokal.

Penelitian ini memuatkan aspirin pada perancah tulang berbasis hidrogel gelatin $CaCO_3$ dengan berat berbeda yaitu 0,5 g; 1,0 g; 1,5 g; dan 2,0 g. Uji *Fourier Transform Infra Red* (FT-IR) dilihat pada rentang bilangan gelombang 700 cm^{-1} sampai 4000 cm^{-1} untuk melihat perubahan struktur setelah sintesis pemuatan aspirin ke dalam hidrogel gelatin $CaCO_3$. Uji pelepasan obat dari perancah setelah perendaman dalam larutan *phosphate buffer saline* (PBS) pada jam ke 1, 3, 6, 8, 10, 12, 24, 26, 28, 30, 32, 48, dan 54, menggunakan spektrofotometer panjang gelombang 296 nm. Uji *in vitro* viabilitas sel preosteoblas MC3T3E1 dengan MTT *assay* dilakukan setelah inkubasi 24 jam pada konsentrasi 1,5; 3; 6,25; 12,5; 25; 50; 75; 100 µg/ml. Uji *in vivo* dengan cara implantasi subkutan selama 3 hari pada punggung tikus Wistar usia 3 bulan, berat 300-350 g dilakukan untuk melihat efek aspirin terhadap penurunan sel inflamasi akut (neutrofil). Pemeriksaan histologis dengan pewarnaan HE dan pengamatan diambil pada 10 lapang pandang menggunakan mikroskop cahaya dengan tambahan Optilab® pada perbesaran 400X13.

Hasil penelitian menunjukkan bahwa sintesis pemuatan aspirin dalam hidrogel gelatin $CaCO_3$ terbukti tidak mengubah struktur kimia pada gugus aktif karbonil dan karboksil dari aspirin. Rata-rata pelepasan aspirin secara *prolonged release* dari perancah pada semua kelompok berkisar selama ±52 jam. Uji viabilitas sel, menunjukkan hanya kelompok Aspirin 0,5 g dan 1,0 g yang dianggap aman bagi sel karena rerata viabilitas sel di atas 50% tetapi perbedaan pengaruh antara kedua kelompok tersebut tidak signifikan ($p>0,05$). Hari ke-3 pasca implantasi, aspirin mampu menurunkan rerata jumlah sel inflamasi akut (neutrofil) secara signifikan dibandingkan kontrol ($p<0,05$). Kelompok Aspirin 1,0 g pengaruhnya lebih besar daripada kelompok Aspirin 0,5 g dalam menurunkan sel neutrofil, tetapi perbedaan pengaruhnya tidak bermakna secara statistik. Berdasarkan hasil penelitian yang dilakukan, dapat disimpulkan bahwa pemuatan aspirin pada perancah hidrogel gelatin $CaCO_3$ dapat menghasilkan efek pelepasan lokal terkendali yang baik untuk mengatasi rasa sakit pasca bedah akibat reaksi inflamasi. Pemuatan aspirin dengan berat 0,5 dan 1,0 g diketahui aman bagi sel dan mampu menurunkan sel neutrofil.

Kata kunci : Aspirin, NSAID, antiinflamasi, hidrogel, $CaCO_3$.

ABSTRACT

Human body responds to open wound caused by an implantation with a series of wound healing processes, which begins with an inflammatory reaction that triggers post-surgery pain. Doctors usually prescribe non-steroidal anti-inflammatory drug (NSAID) to counter post-surgery pain, such as aspirin. One side effect of using NSAID orally is the occurrence of peptic ulcers. The purpose of this study was to examine the effects of changing the route of giving aspirin from oral to local by means of loading aspirin into a $CaCO_3$ gelatin hydrogel scaffold in accordance with Drug Delivery System (DDS) principle. The change in administering aspirin is expected to have a stronger and faster effect on the target area and prolonged release capability, thereby reduces the systemic side effects and local toxicity.

In this study, aspirin was loaded into four $CaCO_3$ hydrogel gelatin based bone scaffolds of different quantities, namely 0.5 g; 1.0 g; 1.5 g; and 2.0 g respectively. A Fourier Transform Infra Red (FT-IR) test was performed in the wave number range of 700 cm^{-1} to 4000 cm^{-1} to observe any structural changes after the aspirin was synthesized into the hydrogel gelatin $CaCO_3$. A Test on the drug release from the scaffolds after being immersed in the phosphate buffer saline (PBS) solution for 1, 3, 6, 8, 10, 12, 24, 26, 28, 30, 32, 48, and 54 hours was performed using UV-Vis spectrophotometer at 296 nm. An in vitro viability test of MC3T3-E1 preosteoblast cells by MTT assay was carried out after 24 hours-incubation at different concentrations of 1.5; 3; 6.25; 12.5; 25; 50; 75; 100 µg/ml. An in vivo test through a three-day subcutaneous implantation on the backs of three month old Wistar rats weighing 300-350g was done to observe the effects of aspirin on the reduction of acute inflammatory cells (neutrophils). Histological examination with HE staining and observations were carrief out in ten fields of view using the light microscope with an addition of Optilab® at 400X13 magnification.

The results showed that the synthesis of aspirin loading into hydrogel gelatin $CaCO_3$ did not change the chemical structure of the active carbonyl and carboxyl groups of aspirin. The rate of prolonged release of the scaffold in all groups was ± 52 hours. From the cell viability test, only the 0.5 g and 1.0 g Aspirin groups were considered safe for cells because the mean of cell viability was above 50% but the difference in effect between the two groups was not significant ($p > 0.05$). On day 3 post implantation, aspirin was able to significantly reduce the mean number of acute inflammatory cells (neutrophils) compared to controls ($p<0.05$). The 1.0 g Aspirin group had a greater effect than the 0.5 g Aspirin group in reducing the number of neutrophil cells, but the difference in the effect was not statistically significant. Based on the results of the research conducted, it can be concluded that loading aspirin on the $CaCO_3$ gelatin hydrogel scaffold can produce a controlled local release effect which is good for treating post-surgical pain due to inflammatory reactions. Aspirin loading weighing 0.5 g and 1.0 g is known to be safe for cells and can reduce neutrophil cells.

Keywords : Aspirin, NSAID, anti-inflammation, hydrogel, $CaCO_3$