NANO-ENCAPSULATION OF PARACETAMOL IN L-POLY LACTIC ACID USING SUPERCritical ANTI-SOLVENT METHOD

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The present work demonstrates and discusses the encapsulation of a model drug using a supercritical anti-solvent method (SAS). In this study, paracetamol was chosen as a model drug and was encapsulated in the poly L lactic acid (L-PLA), a semi crystalline polymer, under different process parameters namely pressure, temperature, and polymer concentration. The produced nanoparticles were completely spherical with very small size (300 nm) and narrow distribution. Also, the optimum process parameters to produce the smaller particle size were studied by response surface methodology (RSM)
statistical software. The nano encapsulated paracetamol release profile demonstrated a long and sustained release of drug in which 70% of paracetamol release was recorded in 4 weeks. The drug release profile of paracetamol inside the PBS buffer solution was fitted with Korsmeyer Peppas kinetic model based on the $R^2$ value equal to 0.987. The first burst happened after 1 week. The size and morphology of the encapsulated nanoparticles were characterized by scanning electron microscopy. Transmission electron microscopy (TEM) revealed the internal structure of nano-encapsulated paracetamol and verified the full coating of the drug particle with biodegradable polymer. The results demonstrated that increasing the pressure and decreasing the temperature reduce the mean particle size. These results also showed that the particle size is influenced by the degree of super-saturation and initial polymer concentration, simultaneously. Thus, it is crucial to balance the rate of crystallization and the rate of growth. The optimum process parameters to produce minimum mean particle size (301nm) were obtained at 120 bar, 30°C, and 16 ppm polymer concentration based on both SEM images and statistical analysis. The thermal characteristics of nano-particles were investigated via differential scanning calorimetry (DSC) and thermo gravimetric analysis (TGA). The TGA characteristics of nanoparticles were similar to the TGA characteristic of pure polymer due to the higher ratio of polymer in solute. Conversely, the DSC characteristics of nano-particles were similar to paracetamol characteristic due to the higher heat capacity of paracetamol. Based on the DSC thermograms, the intensity of the endothermal melting peak of pure paracetamol was considerably reduced during SAS process due to the changing of nano-particles structure with respect to the pure L-PLA. This issue was also confirmed by the X-ray diffraction pattern as well. All peaks related to both polymer and drug crystallographs were exhibited in the nano-particles crystallography. Fourier transform infrared spectroscopy (FTIR) investigated the
chemical composition of nano-encapsulated paracetamol inside L-PLA. The positions of spectra peaks in FTIR for the encapsulated paracetamol were similar to the absorption peaks of pure polymer due to the high ratio of polymer over drug. The stability of nanoparticles demonstrated by high negative electric charge (-33 ± 3 mV) on the surface of nano particles was confirmed by means of zeta potential characteristic. This high negative surface charge may be due to the presence of carboxyl end groups of L-PLA chain.
Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Master Sains

PENKAPSULAN NANO PARASE TAMOL DI DALAM ASID L POLI LAKTIK MENGGUNAKAN KAEDAH GENTING ANTI PELARUT

Oleh

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Mac 2011

Pengerusi: Profesor Madya Robiah Yunus, PhD

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Kajian ini menunjukkan dan membincangkan pengkapsulan model ubat menggunakan kaedah genting anti-pelarut (SAS). Dalam kajian ini, parasetamol dipilih sebagai model ubat yang dikapsulkan di dalam L-PLA (asid L-poli laktik), suatu polimer semi kristal, di bawah parameter proses yang berbeza iaitu tekanan, suhu dan kepekatan polimer.

Partikel nano yang dihasilkan adalah berbentuk sfera sepenuhnya bersaiz sangat kecil (300 nm) dan pengagihan sempit. Parameter proses yang optimum untuk menghasilkan saiz partikel yang lebih kecil dikaji menggunakan perisian komputer statistik RSM. Profil pembebasan partikel nano parasetamol menunjukkan pembebasan ubat yang lama dan tertahan di mana 70% pembebasan parasetamol dicatatkan dalam tempoh 4 minggu.

negatif yang tinggi (-33 ± 3 mV), telah dipastikan dengan ciri-ciri potensi zeta. Cas permukaan negatif yang tinggi ini boleh diterangkan dengan kehadiran kumpulan berfungsi karboksil pada hujung rantaian L-PLA.
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All praises and thanks be to Allah (S.W.T), who has guided me to complete this study, never could I have found guidance, were it not that Allah had guided me!

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I certify that a Thesis Examination Committee has met on 24 March 2011 to conduct the final examination of Mahshid Kalani on her thesis entitled “Nano-Encapsulation of Paracetamol in L-Poly lactic Acid using Supercritical Anti-Solvent Method” in accordance with the Universities and University Colleges Act 1971 and the Constitution of the Universiti Putra Malaysia [P.U.(A) 106] 15 March 1998. The Committee recommends that the student be awarded the Master of Science.

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DECLARATION

I declare that the thesis is my original work except for quotations and citations which have been duly acknowledged. I also declare that it has not been previously, and is not concurrently, submitted for any other degree at Universiti Putra Malaysia or at any other institution.

MAHSID KALANI

Date: 24 March 2011
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