CONTROLLED-RELEASE PROPERTY OF POLY(METHYL VINYL ETHER-CO-MALEIC ANHYDRIDE) MATRIX

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BY :

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Tarikh : 23 Mei 2004

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Tuan

TAJUK PROJEK: CONTROLLED-RELEASE PROPERTY OF POLY (METHYL VINYL ETHER-CO-MALEIC ANHYDRIDE) MATRIX

Dengan hormatnya perkara di atas adalah dirujuk.

Sukacita dimaklumkan bahawa Mesyuarat Jawatankuasa Penyelidikan ke-71 pada 14 Mei 2004 telah membuat keputusan:

i. Bersetuju meluluskan cadangan penyelidikan yang telah dikemukakan oleh tuan dan Dr Yolande Anthony.

ii. Tempoh projek penyelidikan ini ialah **12 bulan**, iaitu bermula **1 Jun 2004** hingga **31 Mei 2005**.

iii. Kos yang diluluskan ialah sebanyak **RM 50,000.00** sahaja dari Geran MOE. Penggunaan geran yang diluluskan hanya akan diproses setelah perjanjian ditandatangani.

iv. Tuan perlu membelanjakan **50%** daripada geran penyelidikan yang telah diluluskan bagi projek tuan dalam tempoh **6 bulan** pertama projek berjalan. Sehubungan itu, pihak IRDC akan memantau penggunaan geran penyelidikan tuan untuk memastikan 50% daripada jumlah geran yang diluluskan telah dibelanjakan sehingga bulan **Nov 2004**.

v. Semua pembelian peralatan yang kosnya melebihi RM 500.00 satu item perlu menggunakan Pesanan Jabatan Universiti Teknologi MARA (LO). Pihak tuan juga dikehendaki mematuhi peraturan penerimaan peralatan. Panduan penerimaan peralatan baru dan pengurusannya, dilampirkan.

vi. Semua peralatan/kelengkapan penyelidikan yang dibeli adalah menjadi hak milik fakulti. Semua peralatan/kelengkapan hendaklah diserahkan kepada pihak fakulti setelah tamat penyelidikan untuk kegunaan bersama.

vii. Seperti yang tuan sedia maklum tuan perlu membentangkan kertas kerja di Seminar Hasil Penyelidikan IRDC setelah projek tamat dijalankan nanti.

viii. Kertaskerja boleh dibentangkan di seminar selain daripada yang dianjurkan oleh IRDC setelah 75% deraf awal laporan akhir projek dihantar ke IRDC untuk semakan. Walaubagaimanapun, tuan perlu membuat permohonan kepada pihak kami.

Tarikh : 2 March 2007
No. Fail Projek : 600-IRDC/ST5/3/713

Penolong Naib Canselor (Penyelidikan)
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Y.Bhg. Prof.,

LAPORAN AKHIR PENYELIDIKAN "CONTROLLED-RELEASE PROPERTY OF POLY(METHYL VINYL ETHER-CO-MALEIC ANHYDRIDE) MATRIX"

Merujuk kepada perkara di atas, bersama-sama ini disertakan 3 (tiga) naskah Laporan Akhir Penyelidikan bertajuk "Controlled-release property of poly (methyl vinyl ether-co-maleic anhydride) matrix".

Sekian, terima kasih.

Yang benar,

WONG TIN WUI
Ketua
Projek Penyelidikan

ABSTRACT

The drug release behavior of beads made of poly(methyl vinyl ether-co-maleic acid) was investigated with respect to the influence of microwave irradiation. The beads were prepared by an extrusion method with sodium diclofenac as a model water-soluble drug. The beads were subjected to microwave irradiation at 80 W for 5 and 20 min, and at 300 W for 1 min 20 s and 5 min 20 s. The profiles of drug dissolution, drug content, drug-polymer interaction and polymer-polymer interaction were determined by dissolution testing, drug content assay, differential scanning calorimetry and fourier transform infra-red spectroscopy. Keeping the level of supplied irradiation energy identical, treatment of beads by microwave at varying intensities of irradiation did not bring about similar drug release profiles. The extent and rate of drug released from beads were markedly enhanced through treating the samples by microwave at 80 W as a result of loss of polymer-polymer interaction via the $(CH_2)_n$ moiety, but decreased upon treating the beads by microwave at 300 W following polymer-polymer interaction via the O-H, COOH and COO^- moieties as well as drug-polymer interaction via the N-H, O-H, COO^- and C-O moieties. The beads treated by microwave at 300 W exhibited a higher level of drug release retardation capacity than those of treated by microwave at 80 W in spite of polymer-polymer interaction via the $(CH_2)_n$ moiety was similarly reduced in the matrix. The mechanism of drug release of both microwave-treated and untreated beads tend to follow zero order kinetics. The drug release was markedly governed by the state of polymer relaxation of the matrix and was in turn affected by the state of polymer-polymer and/or drug-polymer interaction in beads.

Key Words: Drug-polymer interaction; Microwave; Polymer-polymer interaction; Poly(methyl vinyl ether-co-maleic acid).

INTRODUCTION

Carbohydrate polymers, such as alginate and pectin, are widely used in the design of drug delivery systems for small molecule drugs (Fu Lu *et al.* 1991, Wan *et al.* 1993, Ashford *et al.* 1994, Wan *et al.* 1994, Adkin *et al.* 1997, Chan *et al.* 1997, Macleod *et al.* 1997, Munjeri *et al.* 1997, Sriamornsak *et al.* 1997, Fundueanu *et al.* 1998, Pillay *et al.* 1998a, b, Sriamornsak and Nunthanid 1998, Acarturk and Takka 1999, Liu and Krishnan 1999, Pillay and Fassihi 1999, Takka and Acarturk 1999, Gupta *et al.* 2001, Chan and Heng 2002, El-Gibaly 2002, Wong *et al.* 2002a, b, c, Murata *et al.* 2004, Nurjaya and Wong 2005, Wong *et al.* 2005). Nonetheless, the embedded drug molecules exhibit a fast rate of drug release via diffusion through the pores of the matrix. Such rate of drug release is undesirable in the case of the need to target the drugs to the lower part of gastrointestinal tract, particularly, the colon. As such, various formulation and processing approaches have been taken to negate the rate of drug release from these polymeric matrices. The latest processing approach lies in the application of microwave technology to modify the state of molecular interaction between the polymer chains (Wong *et al.* 2002c, 2005, Nurjaya and Wong 2005). Under the influence of microwave irradiation, it is found that the drug release could be further retarded in the matrix made of alginate through changing the profiles of polymer crosslinkage and complexation. Nevertheless, the treatment of pectinate matrix by microwave brings about the higher extent and rate of drug release.

Poly(methyl vinyl ether-co-maleic acid) and analogs are used as thickening agent, encapsulating agent, denture adhesive as well as adjuvant for transdermal drug delivery system (Matsuya *et al.* 1996, Arbós *et al.* 2002, 2003, Luppi *et al.* 2003, Kockisch *et al.* 2004, Owens *et al.* 2005, Salman *et al.* 2005). The wide application of