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An investigation into the drug dependence of the structure and release properties of Gelucire 50/13 matrices

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Gelucires ® are pharmaceutical excipients composed of glycerides, free fatty acids, PEG esters and free PEG. The wide range of components which constitute the gelucires results in physical as well as chemical complexity, e.g. Sutananta et al (1995); Remunan et al (1992). The objective of this work was to study the effects of incorporating different drugs have on the structure of gelucire itself and the subsequent effects on release. Gelucire 50/13 (Gattefosse, St.Priest) and the model drugs anhydrous caffeine and paracetamol (Avocado, Lancs.) were selected. Comminuted samples of pure G50/13 and 10% drug dispersions were placed on a microscope slide and subjected to a 2°C/min heating and cooling cycle using Mettler FP52 hot-stage. Changes to the structure were observed using an Olympus BX50 light microscope fitted with Differential Interference Contrast (DIC) prisms. For DSC, the samples were sealed in aluminium non-hermetic pans and scanned at 2°C/min using TA Instruments DSC 2920. Dissolution studies were carried out in USP rotating basket apparatus (PTW S Dissolution test instrument, Pharmatest) on tablets fabricated by the hot fusion method, to see whether structural changes to the gelucire base affect the drug release.

HSM showed that both paracetamol and caffeine dissolved to a limited extent in the base but paracetamol caused a different form of the matrix to crystallise compared to the pure G50/13; caffeine recrystallised as a separate phase and caused no discernible change to the Gelucire. DSC studies (Figure 1) showed that the profile for the caffeine dispersion was similar to the pure G50/13 but the profile for the paracetamol dispersion was markedly different, with the ΔH_f for the first gelucire melting peak for the paracetamol sample being greater than for caffeine or drug-free sample. This indicates that paracetamol may be stabilising a metastable form of the gelucire. Dissolution studies indicated that the caffeine sample has a higher rate of release than the paracetamol sample (Figure 2). Since both drugs have similar water solubility in water (caffeine 1 in 60 and paracetamol 1 in 70), the difference in release may be at least partially due to the effects that drugs have on the gelucire matrix.

Figure 1: DSC thermal profiles of the pure G50/13, 10% caffeine in G50/13 and 10% paracetamol in G50/13 samples

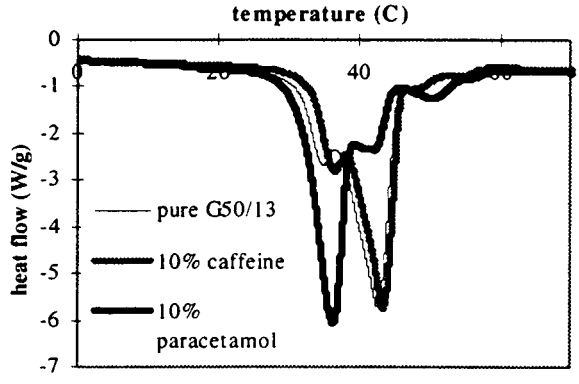
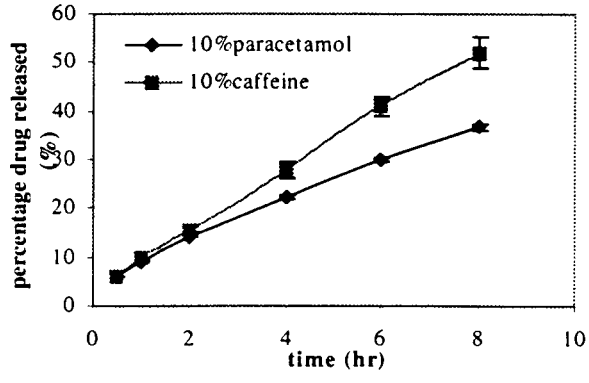


Figure 2: Dissolution profiles of 10% caffeine in G50/13 and 10% paracetamol in G50/13.



In conclusion, this work has demonstrated that the choice of drugs is of importance when ascertaining the physical structure and drug release profile of the gelucire matrices.

Sutananta, W., et al. (1995) J. Pharm. Pharmacol. 47: 182-187
Remunan, C., et al. (1991) Int. J. Pharm. 80: 151-159