

**INFLUENCE OF PEG GRADE AND DRUG CONCENTRATION ON THE DRUG
CRYSTALLINITY OF METRONIDAZOLE-PEG SOLID DISPERSIONS PRODUCED BY
HEAT FUSION**

Ching Mien Oh, Paul Wan Sia Heng, Paul and Lai Wah Chan

GEA-NUS Pharmaceutical Processing Research Laboratory, Department of Pharmacy,
National University of Singapore, 18 Science Drive 4, 117543 Singapore.

Email: a0026784@nus.edu.sg

ABSTRACT

Polyethylene glycol (PEG), a hydrophilic polymer, is frequently used as a drug carrier to improve the dissolution of poorly water-soluble drugs. This study aimed to investigate the impact of different grades of PEG (1500, 3350 and 6000) on the crystallinity of metronidazole existing in various concentrations (10 to 60 %) in the formulation. The solid dispersions were prepared by heat fusion and milled down to microparticles for characterization by powder x-ray diffractometry. Viscosity measurements were also carried out on the molten mixtures at different temperature. Irrespective of the PEG grade, the reduction in drug crystallinity increased when the drug concentration was raised from 10 % to 20 %. Further increase in drug concentration from 20 % to 50 % was observed to increase the viscosity of the molten mixture markedly but the reduction in drug crystallinity remained relatively constant. At low drug concentration (<20 %), the very slight difference in viscosity affected drug crystallinity markedly. At high drug concentration, the viscosity effect was minimal. The findings suggested a dynamic system where the drug was continually thrown in and out of the PEG phase, and the existence of a critical viscosity that restricted the motility and promoted bond formation between drug molecules. This aptly accounted for the lowest reduction in drug crystallinity due to PEG 6000, followed by PEG 3350 and PEG 1500. At high drug concentrations where the critical viscosity was exceeded, further increase in viscosity would not have any significant effect on the drug crystallinity.

Reproduced with permission of copyright
owner. Further reproduction prohibited
without permission.