THE EFFECT OF SOLID STATE CHANGES AND PHYSICAL INTERACTIONS WITH EXCIPIENTS ON THE DISSOLUTION BEHAVIOUR OF CARBAMAZEPINE TABLETS

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Materials and Methods

Materials
CBZ form II and DH powder, CBZ form III and DH compacts (400 mg), hydroxypropyl methylcellulose (HPMC) (Mw 26,000 Da), and polyethylene glycol (PEG) (Mw 4,000 Da).

Methods
All dissolution tests were performed using USP apparatus 2 (paddle method) at 50 rpm and 37°C. A 24-station dissolution apparatus (D800 dissolution tester, Logan Instrument Corp.) with 200 ml dissolution media (distilled water, PEG solution, and HPMC solution). The dissolved concentration of CBZ in each medium was determined by high performance liquid chromatography (HPLC).

Results and Discussion

Compacts prepared from CBZ form III
The dissolution profiles of CBZ form III compacts in various dissolution media are shown in Figure 1.

Figure 1. Dissolution profiles of CBZ form III compacts in three different dissolution media: water (A), PEG solution (B), and HPMC solution (C). Bars: 200 µm.

The concentration of CBZ dissolved decreased with the increase in time in all media. However, the dissolution rate was significantly higher in PEG solution compared to water and HPMC solution. The dissolution rate in PEG solution was much higher compared to that from CBZ compacts in the first 150 min (Figure 1A). This suggests that PEG may have induced a high surface absorption of the HPMC onto the CBZ particles, resulting in a slower dissolution rate in the PEG solution than in water.

Conclusions
This study has investigated the dissolution of CBZ and DH compacts in water and two excipient solutions: PEG and HPMC solutions (0.1% w/v) using SEM as an important complementary tool to observe morphology changes during the entire dissolution process. SEM proved to be invaluable for interpretation of the results. Although the dissolution of these compacts in various dissolution media are all complex processes with many contributing factors (type of crystalline form, CBZ or DH, crystal morphology, surface area, and excipient interactions with drug particles), the influence and relative importance of these factors on the resulting dissolution profiles of CBZ and also DH compacts were clarified.

References