Enhanced Aqueous Stability of Acid-Labile Drug Using Alkalizer-Containing Solid Dispersion
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**Purpose**
To investigate the new mechanistic evidence regarding the effects of pharmaceutical alkalizers on the stability of esomeprazole magnesium dihydrate (EPM), a proton-pump inhibitor (PPI), in gastrointestinal fluid.

**Methods**
The alkalizer-added solid dispersion was prepared by dissolving (or dispersing) EPM, alkalizer, and Opadry® (HPMC 6 cps), in ethanol 50% (v/v) followed by spray drying. Nine different alkalizers were assessed for *in vitro* stability in two media, gastric fluid (pH 1.2 buffer) and intestinal fluid (pH 6.8 buffer). The microenvironmental pH (pHM), drug crystallinity and morphology of pure drug and drug-loaded solid dispersions with or without alkalizer were examined by differential scanning calorimetry (DSC), powder X-ray diffraction (PXRD), and scanning electron microscopy (SEM). The molecular interactions among drug, carriers, and alkalizers in solid dispersions were elucidated by Fourier transform infrared spectroscopy (FT-IR).

**Results**
MgO proved to be the best alkalizer to stabilize EPM in both gastric and intestinal fluids when incorporated into the EPM-loaded solid dispersion. pHM values of alkalizer-containing solid dispersions were significantly higher than that of the solid dispersion without alkalizer. The pHM values decreased in the following order: MgO (6.36 ± 0.20), Na₂CO₃ (5.75 ± 0.25), Ca(OH)₂ (5.22 ± 0.40), and without alkalizer (4.71 ± 0.26). DSC and PXRD data exhibited a change in the crystallinity of EPM, from crystalline to amorphous form, in solid dispersion. FT-IR indicated a strong molecular interaction among EPM, alkalizer and polymer; in particular, MgO showed the strongest interaction with EPM. SEM images demonstrated a relatively spherical shape of MgO-incorporated solid dispersion compared to the less-defined shape of pure drug.

**Conclusion**
This study provides a promising approach for stabilization of acid-labile drugs (EPM) by utilizing alkalizer-containing solid dispersion, which would be helpful for improving the drug oral bioavailability.