Development of a Multivariate FTIR Spectroscopic Technique to Investigate Extent of Cross-Linking in Soft Gelatin Capsules
M. Harati, D. Durham, O. Van Cauwenberghe
Accucaps Industries Ltd.

Purpose
Understanding the physical and chemical cross-linking phenomenon is extremely important in formulation of new products to take measures to minimize it. Attenuated Total Reflection Fourier Transform Infrared (ATR-FTIR) spectroscopy and Ultra Performance Liquid Chromatography (UPLC) methods are developed to compare and correlate extent of cross-linking with dissolution performance of SGCs. The purpose of this study is to 1) evaluate the potential of FTIR spectroscopy for analyzing formaldehyde-induced cross-linking of SGCs and 2) to develop a multivariate approach to estimate the extent of cross-linking to provide more understanding on its mechanism.

Methods
In this study, formaldehyde is used to cross-link gelatin capsules and degree of cross-linking. Fresh empty shells and Omega-3 capsules were exposed to formaldehyde vapor to achieve various degrees of cross-linking. Also, aldehydes were added into the encapsulated fill to determine the effect of aldehydes on crosslinking and the determination of the extent of crosslinking of the interior of the shell. The FTIR spectra were acquired immediately after formaldehyde exposure with 36 scans at 4 wavenumber resolution. UV spectroscopic detection is additionally used to gain quantitative data about fill material dissolution and complement observation from FTIR spectroscopic measurements. Sampling for dissolution profile was done at 10, 20, 30, 45, 60, 90, and 120 min.

Results
Dissolution result of induced cross-linking using 1% formaldehyde shows that about 90% of the fill material was dissolved during 120 min while dissolved omega-3 percentage decreased to slightly less than 50 when formaldehyde concentration increased to 10%. Furthermore, induced cross-linking become very extensive in the presence of 20% formaldehyde solution for 24 hours which does not allow SGCs to rupture and subsequently dissolve. Developing an ATR-FTIR technique, we were able to reveal a correlation between changes of 1620 and 1550 cm⁻¹ band and dissolution results.

Conclusion
In conclusion, our FTIR results coupled with UPLC data indicates that this approach is promising techniques to provide new insights into extend and mechanism of SGC's cross-linking under a range of different formaldehyde vapor concentrations.