

Application Note — Monitoring Reverse Phase LC of Acetonitrile/Water in Pharma Applications

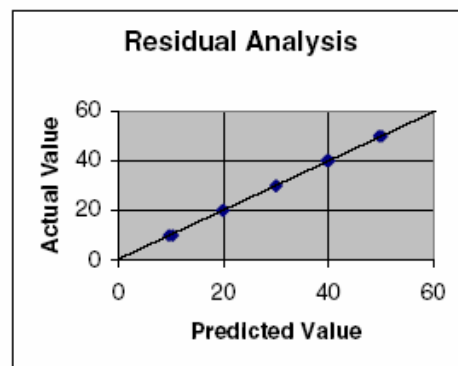
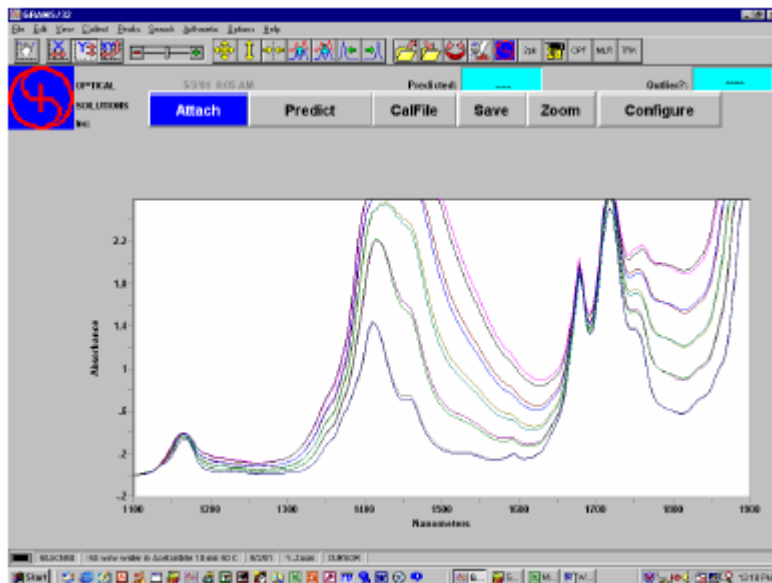
Purpose: To provide continuous monitoring of acetonitrile (ACN):water mobile phase gradients utilized in prep scale reverse phase chromatographic separation of active pharmaceutical ingredients with a NIR ClearView® or ChemView® fiber optic filter photometer.

Experimental: Our PS-2E diode array spectrophotometer was used to measure the NIR spectra of ACN:water mixtures to select wavelengths for our process photometers. Two meters of low-OH fiber optic cables were used and the samples were measured in a 10 mm quartz cuvette in our HeaterCell accessory at 40 and 50 °C.

Results: The resulting PS-2E spectra are shown at top right for 10, 20, 30, 40 and 50 wt. % water in ACN. The main water peak near 1420 nm is off-scale for the 10 mm optical path selected. The alternative would be to use a 1 or 2 mm optical path to keep this peak on scale. Such a narrow optical path is difficult to clean in a process probe and may entrain bubbles. The slightly different curves at each concentration reflect the effect of sample temperature on the water spectrum.

Our OS-MLR program in our GRAMS operating system in the PS-2E selected two wavelengths for calibration. The calibration model also includes a coefficient for sample temperature. The predicted vs. actual plot at middle right shows an excellent calibration with an R2 of 0.9997 and a standard error of 0.3% water. The temperature coefficient indicates a correction of 0.15% water/°C. The coefficients for each of the two wavelengths are nearly equal and opposite in sign. This means that the already low photometric drift in our SMART PHOTOMETERS™ will nearly cancel. The long-term drift of 1-2 mAU thus corresponds to a precision of 0.02 to 0.04% water.

Discussion: The use of two analyzing wavelengths allows our ChemView® photometer to additionally perform chemical outlier detection along with the water measurement. If that is not required, then our low cost ClearView® photometer can readily make this measurement. Both systems employ direct insertion fiber optic probes or flow probes for bypass streams. Our Simulplex™ ChemView® photometer can measure two independent fiber optic probes at the same time. Our systems have also undergone life cycle validation.



ChemView
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(EEx/d IIB) Enclosure



ClearView
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