ROLE OF INFRA-RED ANALYSIS IN THE STABILITY EVALUATION OF THIOPHANATE SUSPENSIONS

R S Chawla*, R Whyte, R S Cook, Product Development, Pharmaceutical Division, May & Baker Ltd, Dagenham, Essex, UK.

Assessment of the physicochemical characteristics of dispersed systems may be utilised as predictive models in both the formulation and long-term stability of suspensions (Kreiger (1972), Tadros (1980).
Conventional methods to assess suspension stability involving crystal growth use either changes in rheological parameters or particle size ranges.
However, the methods have several disadvantages, especially in the examination of flocculated systems.
In an attempt to elucidate the probably mechanism of crystal growth in thiophanate suspensions, crystals from the suspension were examined using infra-red spectrophotometry. Particle size was measured using a laser light scattering system (Malvern Instruments). Crystals were extracted by centrifuging the samples at x 2500g for 1 hour and subsequently washing off residual excipients. Examination of the infra-red peak profile suggested various spectral differences in samples where crystal growth was suspected as opposed to control batches. These differences correlated well in comparison to retrospective tests, such as sedimentation and rheological examination. This correlation in conjunction with changes in particle size of the suspension after 1 week may be utilised as a useful predictive test (Table I).

	INFRA-RED SPECTRA				PARTICLE SIZE	
THIOPHANATE	No OF PEAKS AT (nm)				WEIGHT % > 6.4μm	
SUSPENSIONS	λ1	λ2	λ3	λ4		
	600-700	1710	3000	3320	INITIAL	1 WEEK
CONTROL	1	1	2	0	37.0	37.7
FAILED SUSPENSION	3	2	1	1	37.7	65.4

Confirmation of the peak profile was obtained using a computerised Fourier Transform Infra-red system (Perkin-Elmer), which exhibited the difference spectra between the control and samples showing crystal growth. It is proposed that suspension instability, represented by a factor such as crystal growth could be dependent on the composition of the solvation layer surrounding individual particles. This layer could be made up of a combination of solutes including wetting agents or gels incorporated into the suspension. The orientation of these molecules around the particles will influence to a great degree the solubility of the thiophanate, leading to crystal growth.
The appearance of peaks at λ1, λ2, and λ4 suggest that the solvation layer in combination with the incorporated components influences particle suspendability and structure such that it is possible to predict suspension instability by assessing and correlating infra-red spectral characteristics and particle size analysis.
The differential infra-red technique is reasonably simple to apply thus lending itself in combination with particle size analysis as a predictive test in suspension stability; and an adjuvant test for the formulation of stable suspensions.

Kreiger, I M (1972 Adv. Colloid Interface Sci. 3 : 111.
Tadros, Th F (1980) Adv. Colloid Interface Sci. 12 : 141.