THE DETERMINATION OF SULPHOXIDE IN DEGRADED CHLORPROMAZINE FORMULATIONS BY SECOND DERIVATIVE UV-SPECTROPHOTOMETRY

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Phenothiazine formulations may degrade by aerial oxidation to the corresponding sulphoxide, observed as a shoulder near 345nm in the UV-spectrum (Davidson, 1978). The sulphoxide may be assayed by difference spectrophotometry using as reference an equimolar solution of the parent phenothiazine generated by quantitative reduction of the sample (Davidson, 1978). An alternative and simpler approach is to transform the UV-spectrum to its second derivative, $d^2A/d\lambda^2$, (Fell, 1978), when the sulphoxide shoulder near 345nm appears as a characteristically sharp peak, while interference by the parent compound is almost eliminated. The present work describes the development and evaluation of a rapid second derivative spectrophotometric assay for chlorpromazine sulphoxide (CPSO) in fresh and degraded formulations of chlorpromazine hydrochloride (CP).

In a series of binary combinations of CPSO and CP, the CPSO level was varied to give a calibration graph which simulated oxidative degradation of CP from 0 to 30%, the total molar concentration being constant at 0.563mM (corresponding to a 1+24 dilution of CP syrup to give 200 μg CP ml^{-1}). The second derivative spectrum generated by a Hitachi electronic module in series with a Perkin-Elmer Model 200 UV-visible spectrophotometer (scan speed 240nm min^{-1}; spectral band-width 2nm) displays a minimum near 340nm whose amplitude (D_L) measured to the satellite peak near 350nm varies linearly with CPSO concentration, the small negative Y-intercept being equivalent to 1.10 μg CPSO ml^{-1}. At CP degradation levels corresponding to 5% (9.43 μg CPSO ml^{-1}) and 15% (28.3 μg CPSO ml^{-1}), the 95% confidence limits (n=6) were $\pm$0.56 μg ml^{-1} and $\pm$ 0.26 μg ml^{-1} respectively. At a constant level of 28.3 μg CPSO ml^{-1}, D_L varied by $\pm$ 2.40% of its nominal value when the CP content (170 μg ml^{-1}) changed by $\mp$ 30%. This slight inverse dependence of the CPSO amplitude on CP content was compensated by employing a composite standard of CPSO with CP at declared formulation strength to calculate the concentration of test samples. The recovery of 9.43 μg CPSO ml^{-1} added to syrups 2 and 3 was 97.5% and 99.1% respectively, the relative standard deviation (RSD) being 0.59% and 0.25% (n = 5).

One fresh (1) and two degraded samples (2 and 3) of CP syrup (nominally 5 mg ml^{-1}) stored in light-resistant bottles and fresh batches of two commercial CP injections in boxed ampoules (25 mg ml^{-1}) were assayed for CPSO both by the difference method (I) and the proposed method (II), the percentage degradation being calculated relative to label strength.

	Syrup 1		Syrup 2		Syrup 3		Injection 1		Injection 2	
	I	II	I	II	I	II	I	II	I	II
CPSO μg ml^{-1}	146	151	514	509	787	825	2550	2780	2100	2470
% CP degradation	3.1	3.2	10.9	10.8	16.7	17.5	10.8	11.8	8.9	10.5
% RSD (n=5)	10.4	1.03	2.83	1.32	1.29	0.97	10.9	5.36	16.0	5.96

Good agreement between the two methods was observed. Although both injections contained the antioxidants sodium sulphite and sodium metabisulphite, wide inter-vial variation (as RSD) and relatively high CPSO levels were found. This rapid and flexible assay procedure has been used to monitor the oxidative stability of chlorpromazine preparations and, with some modification, formulations of other phenothiazines in filled and partially filled containers during storage.

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