# THE DETERMINATION OF PHENOTHIAZINE SULPHOXIDES IN DEGRADED PHENOTHIAZINE FORMULATIONS

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Application of a specific assay for the determination of phenothiazine drugs in pharmaceutical preparations (Davidson, 1976) has shown that many aqueous formulations which give good results from newly opened containers give low results after storage for several months at room temperature in their partially filled containers. As the loss of active drug is due to aerial oxidation of the phenothiazine to the sulphoxide, the extent of decomposition in these preparations may be assessed directly by assaying the levels of the phenothiazine sulphoxide.

The assay of the sulphoxides is based on a difference spectrophotometric measurement of the absorbance of a solution of the sulphoxide in 0.2N hydrochloric acid relative to an equimolar solution reduced with zinc powder to give the parent phenothiazine. The difference spectrum shows an absorption peak around 345 nm which is proportional to the concentration of the sulphoxide in the unreduced solution. The level of sulphoxide in the sample is obtained by comparison of the difference absorbance of the sample solutions with that of standard sulphoxide solutions. The assay is specific for the phenothiazine sulphoxide in the presence of the unchanged drug, the sulphone, excipients and co-formulated drugs since the spectral properties of these are unaltered by treatment with zinc and hydrochloric acid.

To avoid interference from the colouring agents the sulphoxides in coloured formulations are extracted from alkaline solution into chloroform and then re-extracted into 0.05 M hydrochloric acid giving colourless solutions of the sulphoxide. This procedure separates the sulphoxide from most of the unchanged phenothiazine and permits a larger sample weight of the formulation to be assayed. Levels of sulphoxide as low as 0.5% may therefore be determined in the presence of the unchanged drug.

Several commercial phenothiazine preparations containing the labelled amount of the unchanged phenothiazine when the containers were first opened were stored for periods of up to two years in partially filled containers. The levels of total phenothiazine, i.e. unchanged phenothiazine determined by the method of Davidson (1976) and phenothiazine sulphoxide determined by the present method agree well with the label strength of the formulation, but the proportion present as the sulphoxide was appreciable in some aqueous preparations which had been stored for a long period of time in containers with a large headspace of air. The results for three batches of chlorpromazine syrup (25 mg/5 ml) are recorded in the table.

| Chlorpromazine Syrup Batch | Storage Conditions (in 125 ml Amber bottles) | Unchanged Chlorpromazine % Label | Chlorpromazine Sulphoxide (as Chlorpromazine) % Label |
|---|---|---|---|
| A | ½ full bottle; 11 months | 84.3 | 15.9 |
| B | 1/4 full bottle; 18 months | 78.1 | 21.6 |
| B | 9/10 full bottle; 18 months | 98.0 | 1.6 |
| C | 1/5 full bottle; 18 months | 72.2 | 28.5 |
| C | full bottle; 18 months | 99.5 | 0.8 |

Davidson, A.G. (1976) J. Pharm. Pharmac., 28, 795-800.