LETTER TO THE EDITOR

Interpretation of thermograms of oxytetracycline-excipient mixtures

J. P. REMON, R. VAN SEVEREN, P. BRAECKMAN*, *Laboratory of Galenics and Pharmacognosy, Faculty of Pharmacy, State University of Ghent, Ghent, Belgium*

Recently Lee & Hersey (1977) reported the utility of differential thermal analysis in preformulation stability screening of oxytetracycline tablet formulations. We agree with their view of eliminating possible incompatible excipients by D.T.A. But in the case of oxytetracycline hydrate and oxytetracycline hydrochloride mixtures, we think that the authors conclusions in connection with the endotherms occuring after the decomposition exotherm of the tetracycline compounds are misleading. Besides, those mixtures may contain products, as for example glucose and calcium gluconate, which decompose before tetracycline decomposition. In our opinion the decomposition of the oxytetracyclines eliminates interpretation of later occurring endotherms which could lead to the postulation that a new compound has been detected.

We now report our findings and interpretation of the thermograms. The apparatus used in our laboratory is a Mettler T.A. 2000 analyser, with a constant heating rate of 5° min^{-1}. We worked in a nitrogen atmosphere and used perforated aluminium crucibles. The sensitivity range was 100 μV. The physical mixtures were all equal weight ratio mixtures made with pestle and mortar. The samples weighed ~100 mg. For the experimental parameters we also refer to the publication of Shishkin (1972) who used 20 mg samples and a heating rate of 13° min^{-1}.

We agree with the findings of Lee & Hersey (1977) on pure oxytetracycline dihydrate: a dehydration endotherm at 132° and a decomposition exotherm at 187°, while the hydrochloride only shows a decomposition peak at 212°. Sodium alginate-oxytetracycline hydrochloride mixture gives a supplementary exotherm at 225°, probably due to decomposition of the sugar polymer.

Magnesiumstearate-oxytetracycline hydrochloride mixture gives exothermal peaks at 215·5° and at 217°, while a mixture with stearic acid gives the same thermogram pattern, but with a downward shift of the first exotherm (207·5°). Consequently, the changes seen in the thermogram could not be due to magnesium stearate only, as was concluded by Lee & Hersey (1977) but perhaps to stearic acid. Adding magnesium oxide results in suppression of the dehydration endotherm in the case of oxytetracycline dihydrate and a flattening of the decomposition peaks of both of the compounds. On this matter we refer to the work of Yariv & Mitchell (1967) who studied the influence of inert materials on thermograms.

New endotherms were observed in calcium gluconate-oxytetracycline mixtures at 149° and 161°, but in our opinion these were due only to the calcium gluconate, because there was only a downward shift of respectively 5° and 10° with respect to the thermograms of pure calcium gluconate. This pure calcium gluconate showed a brown colour after the endotherm at 154°, due to the decomposition of the product. In the case of mannitol and glucose we agree with the findings of Lee & Hersey (1977). We also found a broad endotherm between 195° and 205° in the oxytetracycline hydrochloride mixtures. In our findings this endotherm was due to caramelization of these sugar products, followed by a decomposition exotherm. To find out the real influence of calcium ions on oxytetracyclines, we examined the thermograms of pure calcium chloride $2H_2O$, a physical 50% mixture of it with oxytetracycline hydrochloride, and a 40° vacuum-dried solution.

Pure calcium chloride $2H_2O$ shows two endotherms, at 117° and at 135°. Both are due to release of water. The physical mixture shows a downward shift of the decomposition peak (221°), while the vacuum dried product recovered from the solution gives a complete suppression of this exotherm. In this last case only a progressive exothermic change of the base line indicated a slow decomposition of organic material.

October 12, 1977

* Correspondence.

REFERENCES

LEE, K. C. & HERSEY, J. A. (1977). *J. Pharm. Pharmac.*, **29**, 515–516.
SHISHKIN Y. L. (1972). *Khim.-farm. Zh.*, **6**, 60–62.
YARIV, S. & MITCHELL, B. D. (1967). *Chemy Ind. (Lond.)*, 1744–1745.